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NORMAL HISTOLOGY

AND

MICROSCOPICAL ANATOMY

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NORMAL HISTOLOGY

AND

MICROSCOPICAL ANATOMY

BY

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*WITH FOUR HUNDRED AND SIXTY-TWO ILLUSTRATIONS
IN THE TEXT, MANY IN COLOR*



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P R E F A C E

THE appearance of a new text-book in a field which is so inadequately covered as that of normal histology and microscopical anatomy, needs no apology. The rapid development of medical science, by the extensive application of the exact methods of the laboratory, has steadily increased the importance of an accurate and somewhat extended knowledge of microscopical anatomy, until now the medical student finds a ready command of the minute anatomy of the human body to be essential to the satisfactory comprehension of the sciences of physiology, pathology, bacteriology, and clinical medicine. Thus the work of the histological laboratory in American medical colleges has developed within the last two decades from comparative insignificance to an importance which bids fair to rival that of the dissecting room. The aim of the present volume has been to present to the reader a sufficiently comprehensive view of the subject to briefly cover the entire field in which the medical student must now become proficient.

To this end unusual space has been devoted to the microscopical anatomy of those organs which serve as a field for the specialist in medicine. This is especially true of the chapters on the central nervous system, the extreme importance of the histology of these organs, as the very foundation of neurological science, being considered a sufficient warrant for their extended consideration.

In the selection of the illustrations, the aim has been to present exact pictures of actual sections as viewed with known magnification. Unless distinctly described as diagrams, the illustrations invariably represent actual fields in actual preparations, the greater

portion of which have been used for laboratory demonstration in the class room. The magnification in each case is precisely stated.

The original drawings, of which there are about one hundred, have been prepared by the author with the aid of the camera lucida. The photomicrographs, of which one hundred and twenty-two are original, were made, under the author's direction, by Mr. J. N. Lett, and a few by Mr. F. E. Ives. My thanks are due these gentlemen for their able assistance. The illustrations in color have also been drawn by the author with the aid of the camera lucida, and have been reproduced by a process specially devised for the purpose.

I desire at this time to acknowledge my indebtedness for numerous illustrations which have been reproduced from the literature. The author's name has in each case been appended to the legends of these figures, and a reference to the bibliography will serve as a more precise acknowledgment of their source.

The list of literature has been arranged in accordance with the main subdivisions of the text, to facilitate ready reference to special topics, and in the hope that the earnest student may be tempted to search beyond the confines of the text-book, and thus acquire a broader appreciation of the subject. To much of the recorded literature the author has been frequently indebted during his experience as a teacher, and it is a pleasure to be able to gratefully acknowledge his indebtedness to these sources.

A limited chapter on technique has been inserted at the end. The limits of the work do not permit an extended treatise on this subject, a science by itself, but it is hoped that the few fundamental facts which have been briefly stated may serve to give the student a more exact idea of the methods by which tissues are prepared for examination, and the means by which the more important results have been obtained.

Finally, it is a pleasure to acknowledge the repeated courtesies which have been frequently received at the hands of the publishers.

JEREMIAH S. FERGUSON.

NEW YORK.

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NORMAL HISTOLOGY

CHAPTER I

INTRODUCTION—PROTOPLASM—THE CELL

Histology is concerned with the finer structure of living tissues. It may thus include the study of both animal and vegetable tissue.

Animal histology, which deals with the structure of animal tissues, is closely allied to the science of *microscopical anatomy*, which considers the structure of the organs.

All tissues are composed of a living substance called *protoplasm*, which is of very complex structure. It can usually be considered as being made up of certain structural units. These structural units are the animal *cells*.

Protoplasm is capable of all the functions of life—metabolism, motion, growth, development, and reproduction. Thus all protoplasm owes its existence, as does the individual organism also, to a primitive cell mass, the *germ cell*. This germ cell assumes a more or less definite form, which we may consider as the true cell type—the typical cell. The description of the ovum, the germ cell of man, will serve to present those structures which characterize the typical animal cell.

THE TYPICAL CELL.—The term cell, as thus applied, comprises a circumscribed mass of protoplasm. It is enclosed by a membrane of somewhat denser consistence, the *cell wall* or *cell membrane*, which is thickened by a narrow outlying, and often radiating, zone of condensed or otherwise altered protoplasmic substance, the *exoplasm*.

The inner portion of protoplasm, that which surrounds the nucleus and is contained within the cell wall, in contradistinction to the peripheral exoplasm, is called *endoplasm*.

The term *cytoplasm*, though used by Kölliker as synonymous with protoplasm, is now limited, in accordance with the usage of Strasburger, to the entire protoplasmic substance of the cell, exclusive of its nucleus.

The cytoplasm consists of a fluid matrix in which a finely granular reticulum may be demonstrated. Other though less constant structures are found within the cytoplasm. Such are

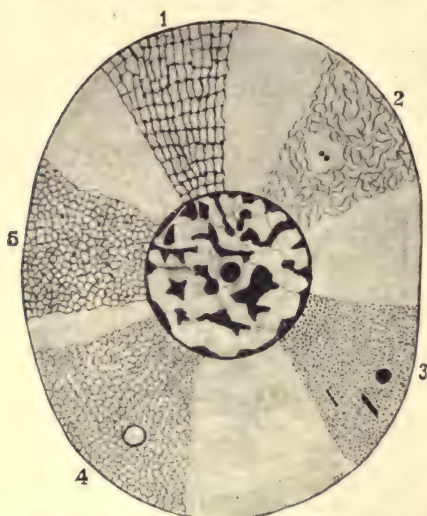


FIG. 1.—DIAGRAM ILLUSTRATING THE VARIOUS THEORIES OF CELL STRUCTURE.

1, alveolar structure; granules occur only at the angles formed by the alveoli. 2, filar structure, showing filar and interfilar mass. The centrosome (a diplosome) is represented in this portion; it is surrounded by a clear attraction sphere. 3, granular structure; coarse microsomes irregularly disposed. This portion contains three foreign bodies which have been included by the cell, a streptococcus, a crystal, and a spheroidal pigment mass. 4, the alveolar walls are formed by regularly arranged microsomes; a vacuole is shown in this section. 5, reticular structure.

The cell is inclosed by a cell membrane, and contains a central nucleus in which are shown the nuclear membrane, indistinct linin fibrils, deeply stained chromatin in coarse threads and irregular masses (karyosomes), and a centrally situated nucleolus or plasmosome.

the *microsomes*, coarse granules which probably belong to the structure of the protoplasm itself; *vacuoles*, which occur as spherical inclosures of a more fluid substance; *paraplasm*,* a generic term which, in various cells, may include all sorts of foreign bodies, pigment, bacteria, ingested particles of nutritive material, etc.

The *nucleus* is inclosed by a highly chromatic *nuclear membrane*, within which is an achromatic ground substance or *nuclear matrix*, a fine network of achromatic *linin* fibrils, and a coarse network of *chromatin* fibrils. The chromatin fibrils here and there present small knot-like thickenings, or *karyosomes*, which are especially prone to occur just within the nuclear membrane, at the periphery of the nucleus. Within the nucleus is also a minute spherule of chromatic substance, the *nucleolus*, which is closely related to the chromatic nuclear network.

The typical cell also includes, usually at some point near the nucleus, a small chromatic dot or *centrosome*, which is surrounded by a clearer area, the *attraction sphere*. These bodies are closely

* This term has been used by von Kupffer in an entirely different sense, as synonymous with exoplasm.

connected with the processes of reproduction by cell division, *karyokinesis* or *mitosis*. In fact, as the nucleus is to be considered as the controlling center of cell activity, growth, and development—in short, of constructive metabolism—so also is the centrosome, in all probability, to be considered as the dynamic center of the cell, controlling the formation of those mitotic figures which finally result in cell division.

A small, spheroidal, distinctly chromatic body is also frequently seen in the cytoplasm in the vicinity of the nucleus. This is the true "*nebenkern*" of Bütschli, which has been shown by Platner and La Valette St. George to be the remains of the mitotic nuclear spindle. At times it has a distinctly fibrillar structure.

Protoplasm.—The finer structure of protoplasm, while certain fundamental facts may be readily observed, is open to varied interpretation by different observers. These interpretations have evolved several theories to explain the minute structure of this substance. It is certain

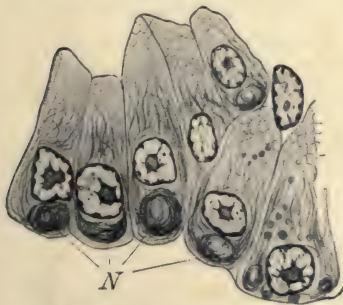


FIG. 3.—EPITHELIAL CELLS FROM THE AMPHIBIAN PANCREAS.

N, *nebenkern*. Highly magnified.
(After Matthews.)

to the latter *hyaloplasm*.* Neither of these structures is, however, of homogeneous, nor even of constant composition. The

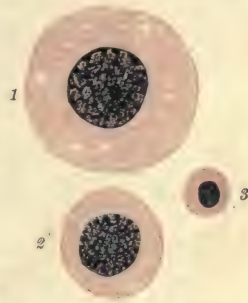


FIG. 2.—VARIOUS SPHEROIDAL CELLS.

1, ovum, from the ovary of a child; 2, spermatocyte; and 3, spermatid, from the testicle of a rabbit. Hematein and eosin. $\times 750$.

that protoplasm, though at times perfectly homogeneous and apparently structureless, upon careful examination usually presents a fine reticulum. It is equally certain that this reticulum is not merely the product of coagulation by strong fixing reagents, for it has been frequently observed in living cells.

Protoplasm may therefore be said to consist of a reticular network and an intervening, fluid, ground substance. To the former Leydig gave the name *spongioplasm*,

* Filar mass and interfilar mass, according to Fleming's theory of the fibrillar structure of protoplasm. The terms mitome and paramitome are also equivalent.

spongioplasm frequently presents a finely granular appearance, which is so universal in its occurrence as to have led to the promulgation of the now discarded granular theory of protoplasmic structure, so ably supported by Altmann. These fine granules, termed *microsomes* by Hanstein, as well as the coarser granules of paraplast, appear to be strictly confined to the spongioplasmic

reticulum, the larger and therefore more frequently observed granules occurring at the intersections of this network (Bütschli).*

There is still some doubt as to the exact character of the reticulum and its matrix, and as to the microscopical substances of which they are the optical expression. All observers are now practically agreed upon the fluid nature of the matrix, or hyaloplasm; the interpretation of the network is still the subject of discussion.

The fibrous nature of this network, though not explaining all the peculiarities of protoplasmic structure, had come to be quite generally accepted, until the convincing studies of Bütschli upon the structure of protoplasm as related to that of certain microscopic oil foams, coagulated proteid solutions, etc., showed that the reticular structure of protoplasm could be almost exactly simulated by the artificial combination of fluids of different consistence to produce a microscopic foam. Bütschli there-

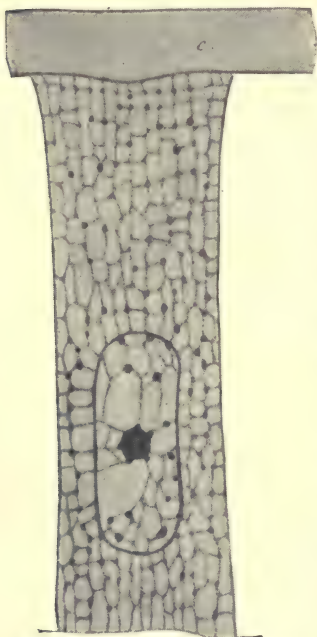


FIG. 4.—AN EPIDERMAL SUPPORTING CELL OF LUMBRICUS TERRESTRIS, ILLUSTRATING THE ALVEOLAR STRUCTURE OF PROTOPLASM.

c, cuticle. Very highly magnified.
(After Bütschli.)

fore regards protoplasm as composed of fluid alveoli of not over 0.001 millimeter in diameter, between and surrounding which is a denser fluid coating, whose section produces the characteristic optical appearance of a true reticulum. That this theory possesses at least a considerable essence of truth is evident from the very able and conclusive demonstrations of its author.

* London, 1894.

Nevertheless, distinct *fibrils* are often to be found in protoplasm, and frequently form an essential part of the cell structure. In this list one finds the neurofibrils of nerve cells which Apathy and Bethe have demonstrated to be frequently continuous from one nerve cell to another; the longitudinal contractile fibrillæ of muscle fibers; the intercellular bridge fibrils of epithelium, which can often be traced through two or three adjacent cells; and finally the intracellular "rod fibrils" of many epithelial cells.

Protoplasm frequently also contains spherical *vacuoles*, which are formed by the accumulation of fluid droplets whose consistence differs from that of the surrounding protoplasm. These droplets may be the result of metabolic activity within the protoplasm itself; they are frequently of a fatty nature.

Other products of cellular metabolism which appear within the cell protoplasm are the *secretory granules*—zymogen, mucinogen, glycogen, etc.—which are formed within the protoplasm of secreting cells.

The **nucleus** differs somewhat in structure from the surrounding cytoplasm. It contains a fluid *nuclear matrix*, or nuclear sap, embedded in which are a chromatic and an achromatic *nuclear network*. The achromatic reticulum is composed of very fine *linin* threads, which form an exceedingly delicate mesh.

The nuclear *chromatin* may or may not exist in the form of a network. Its condition is very variable, and apparently is more or less dependent upon the state of cellular activity as regards the processes of reproduction. The chromatin may thus form a single thread-like fibril of considerable length, which, under high magnification, is seen to be composed of small discoid granules, the *chromomeres* of Fol.

During mitosis the chromatin thread is broken into a given number of V-shaped segments or *chromosomes*; the number of these chromosomes varies in different animals, but is definite for each species. In the resting stage, the phenomena of karyokinesis having been completed, the daughter segments are capable of reuniting to form a single thread, or, on the other hand, they may disintegrate into still smaller granular particles. The granules thus formed are frequently scattered along the linin threads,



FIG. 5.—DEVELOPING FAT CELLS.

The fat droplets, after extraction with alcohol and ether, appearing as vacuoles. Hematein and eosin. $\times 550$.

and often accumulate in knot-like groups to form the *karyosomes*, the larger of which closely simulate the *plasmosomes*, or true *nucleoli*. The chromatin granules are also prone to collect beneath the nuclear membrane, to the inner surface of which they adhere.

Chromatin possesses a strong affinity for basic dyes.* Its granules and threads are often so closely packed as to give to the nucleus the appearance of a solid basophile mass. This condition, however, is only found in the resting nucleus; in those nuclei which are undergoing mitotic changes the chromatin granules are less abundant, less closely packed, and the achromatic portions form a proportionately larger part of the nucleus.

The nucleolus closely resembles the chromatin in its staining properties. It forms a small spherical but solid basophile mass. The nucleolus is described as a plasmosome, to distinguish it from its simulacra, the larger karyosomes. The nucleolus entirely disappears during cell division.

The nuclear wall is likewise only found during the resting stage of the cell as regards the phenomena of karyokinesis. It closely resembles the chromatin, and, though somewhat variable in its staining properties, is, as a rule, strongly basophile. It is said to be composed of *amphipyrenin* (Schwarz †).

Cell Growth, Development, and Differentiation.—The germ cell is not only capable of reproducing itself by karyokinesis, but, in the multicellular animals, is also capable of forming the tissue cells which are so specialized or differentiated as to be no longer capable, like the germ cell, of reproducing the animal species, but which may produce other similar cells to form the various tissues of the body.

In such tissue cells there occur many modifications of the typical cell structure. The exoplasm may be arranged as fibrillæ to form cilia, flagella, intercellular bridges, etc. The shape of the cell may also be altered from its typical contour to a squamous, columnar, polyhedral, fusiform, or even a stellate form, and the cell may be subject to great variations in size.

The endoplasm likewise presents great variations in structure.

* Heidenhain describes the basophile chromatin as *basichromatin*, in contradistinction to the slightly acidophile properties of the exceedingly fine granules which he demonstrated as forming the linin threads, and which he described as *oxychromatin* or *lanthanin*.

† Breslau, 1887.

It may be reticular, alveolar, or homogeneous; it may also contain fibrillæ of considerable length, either straight or coiled, which may even be continued through the exoplasm and into adjacent cells.

The nucleus is also subject to great variations in size, in shape, and in the arrangement of its chromatic fibrils. These changes are in great measure dependent upon the processes of karyokinesis.

As a result of the processes of cell multiplication, which begin with the germ cell, new tissue cells are formed, which exist either as isolated cells, in relation with their neighbors by contact only, or as a continuous protoplasmic mass or *syncytium*, which is formed by fusion of the exoplasm of adjacent cells (Studnička *). The true syncytium is usually found in embryonic tissues; the mature tissues, on the other hand, possess a distinctly cellular character.

The differentiation of cells in the course of development results in the formation of special tissue groups, the protoplasm of each group presenting certain common characteristics. These tissue groups form the *primary tissues* of the body. Thus we distinguish: (1) epithelial tissues, (2) connective tissues, (3) muscular tissues, (4) nervous tissues, (5) blood, (6) lymph.

Still further differentiation may occur within each group. Thus, for example, connective tissue may be fibrous, elastic, areolar, reticular, cartilaginous, bony, etc. These changes, apparently taking place under the influence of the nucleus, are more pronounced at the periphery of the cell. The most marked protoplasmic differentiation is therefore found in the exoplasm—it results in the formation of cilia, intercellular bridges, and the fibrillæ of epithe-



FIG. 7.—A VILLUS OF THE HUMAN PLACENTA, SHOWING A PERIPHERAL SYNCYTIUM OF IRREGULAR THICKNESS.

The connective tissue inclosed by the syncytium contains three capillary vessels. Hematein and eosin. $\times 500$.

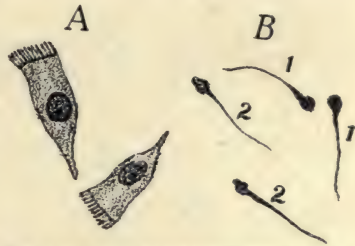


FIG. 6.—CILIAE AND FLAGELLATE CELLS.

A, ciliated cells isolated from the trachea of a cat; B, human spermatozoa—1, in surface view; 2, in profile. Examined fresh in normal saline solution. $\times 550$.

lium, muscle, and connective tissue. Similar differential changes acting upon the endoplasm result in the formation of such structures as the contractile fibrils of muscle cells, the neurofibrils of

nerve cells, the mucin, zymogen and secretory granules of epithelial cells, and the fat of connective tissue cells.

These developmental phenomena are, however, not the only evidence of the vital nature of protoplasm. It presents certain other phenomena, some of which may be microscopically demonstrated, which are accompanied by

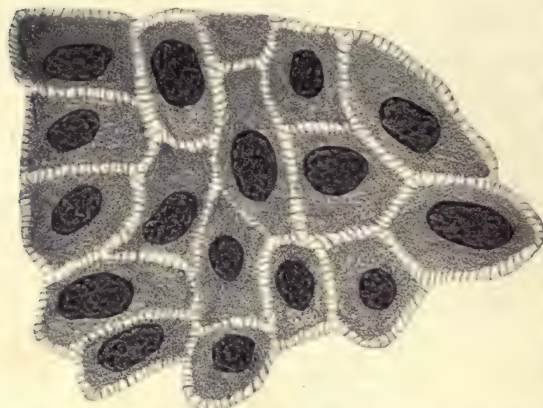


FIG. 8.—GROUP OF EPITHELIAL CELLS FROM THE MALPIGHIAN LAYER OF THE SKIN.

The intercellular bridges are very distinct. Hematein and eosin. $\times 1,000$.

characteristic histological changes. The vital properties which thus concern the histologist are motion, secretion, growth, and reproduction.

Motion.—Cell motion is that evidence of excitability which results in change of the cell form or position. Three varieties may be recognized in animal cells.

(a) *Amœboid Motion*.—This form of cell motion is evidenced by a change of shape of the cell by which protoplasmic processes, *pseudopodia*, are pushed out in one or more directions.

These processes may then be either withdrawn or they may unite with one another, and thus, perhaps, inclose a foreign particle; or, again, the cell body may flow into the pseudopodium, which is thus increased in size, the cell body becoming correspondingly



FIG. 9.—A LEUCOCYTE FROM HUMAN BLOOD IN ACTIVE AMÆBOID MOTION.

The figures indicate the successive forms assumed by the cell. Drawings were made at intervals of one minute. $\times 500$.

thus increased in size, the cell body becoming correspondingly

smaller, until the whole cell finally occupies the position of its former process. The cell has thus changed its position—*locomotion* has been accomplished.

(b) *Ciliary Motion*.—This is a rapid waving motion of fine hair-like cilia which project from the free border of certain cells, as, for example, the ciliated epithelium of the respiratory tract. The rapid undulatory vibrations of the flagellum attached to certain other cells—e. g., the spermatozoa—is closely allied to ciliary motion. The ciliary vibrations are exceedingly rapid, occurring many times to the second.

(c) *Molecular Motion*.—This is a peculiar dancing movement of the finer granules, which occur within cell protoplasm. These granules may be microsomes, various forms of paraplasm, pigment granules, etc. A closely allied form is *pigmentary motion* in which pigment granules, which are at first equally distributed throughout the cell, are collected into a group, which usually surrounds the nucleus; the reverse then occurs, the pigment granules becoming again equally distributed through the cell protoplasm. Molecular motion is readily observed in the pigment granules of the plasmodium malariae, a parasite occurring in the blood of persons afflicted with malarial fever. Molecular motion is closely simulated by *Brownian motion*, a peculiar dancing movement occurring when fine granular particles of inert substance are suspended in a fluid of nearly equal density.

Secretion.—Changes in the appearance of cells may be due to secretory activity. Thus, during rest, glandular cells become distended with their secretion; they appear swollen, and their nuclei are obscured and pushed toward the attached margin of the cell. During activity secreting cells become shrunken and regain their ordinary protoplasmic appearance; their nuclei again approach the center, or even the free margin of the cell.

In other types of secreting gland, as in the sebaceous glands, the secretion is produced by a disintegration of the cell protoplasm, which, in most of these cases, undergoes a fatty metamorphosis.

Growth.—This process involves changes in the size, shape, and consistence of the cell. The increase in size in most cells is not marked. It is, however, frequently sufficient to produce an increased pressure upon surrounding cells, which is to a certain extent accountable for the varying shapes assumed by those cells which are closely packed within the organs of the body. Most cells in their early embryological condition are nearly spherical in

shape. If expansion during the growth of such cells is limited or resisted by surrounding tissues, pressure will be applied to the cell in many directions, and it consequently assumes a polyhedral shape. If, on the other hand, the pressure is excessive in two opposing directions, the cell gradually becomes flattened or squamous. If, again, the pressure on its four sides should exceed

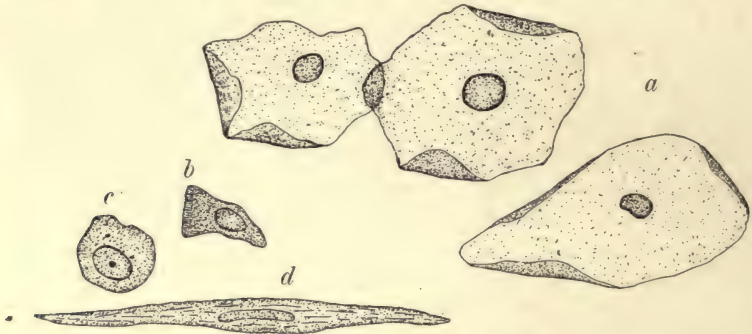


FIG. 10.—VARIOUS FORMS OF CELLS.

a, squamous epithelium from the tongue; *b*, a columnar cell from the small intestine; *c*, a polyhedral or spheroidal cell from the liver; *d*, a smooth muscle cell from the muscular coat of the stomach. $\times 550$.

that applied to the poles of the cell, it would necessarily assume an elongated, prismatic, or columnar shape.

Reproduction.—Two forms of cell division may be observed within the human body: direct division or fission, and indirect division, karyokinesis or mitosis.

Direct Division (*amitosis, fragmentation, fission*).—This method of cell division is the least common. It occurs in some of the epithelial cells of the urinary bladder, in certain cells of red bone marrow, and perhaps occasionally in leucocytes and in glandular epithelium.

The process, according to Nemiloff,* commences by an elongation, followed by constriction, and finally fission of the nucleolus. These changes are accompanied by a similar elongation of the nucleus, followed by constriction and cleavage along such a median plane that a daughter nucleolus is included within each daughter nucleus. The daughter nuclei then travel toward opposite poles of the cell, and constriction and cleavage of the cell protoplasm complete the process.

* Anat. Anz., 1903.

Indirect Cell Division (*karyokinesis*,* *mitosis*†).—This is the usual form of cell division. It consists of a series of changes which chiefly concern the centrosome and nucleus, and which are followed by constriction of the cytoplasm and its final separation into two daughter cells, each of which contains a daughter nucleus and centrosome.

That condition of any cell during which it is not undergoing mitotic change is described as its *resting stage*. In this condition the nucleus is surrounded by a distinct nuclear membrane, within which its chromatic fibrils are irregularly disposed. Near the nucleus is the centrosome, a minute chromatic point which is surrounded by a lighter radiate area, the so-called attraction sphere. It is about the centrosome that the earliest mitotic changes appear. In fact, division of the centrosome itself is fre-

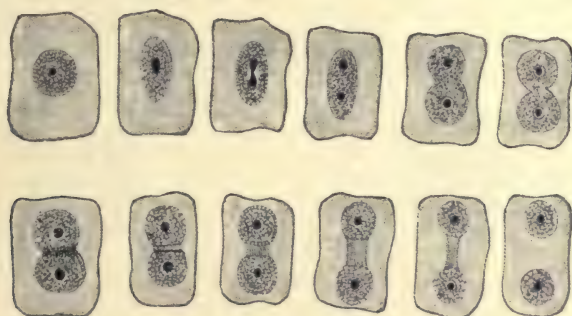


FIG. 11.—DIRECT CELL DIVISION, SHOWING SUCCESSIVE STAGES IN ORDER FROM LEFT TO RIGHT.

(After Nemiloff.) Diagrammatic.

quently the last occurrence in the formation of a daughter nucleus, a “precocious preparation” for future division.

The mitotic changes which accompany indirect cell division may be conveniently considered under four heads: prophase, metaphase, anaphase, and telophase.

Prophase.—The preparatory changes which indicate the approach of cell division begin with the early cleavage of the centrosome, which often even precedes the resting stage. With beginning mitotic activity the daughter centrosomes move apart, each surrounded by its clear radiate, or “astral” attraction sphere.

* Meaning nuclear change.

† A thread, referring to the appearance of the nucleus.

The two asters thus formed may occasionally retain their connection with one another, by means of fine achromatic fibrils which pass from one aster to the other, thus early forming the achro-

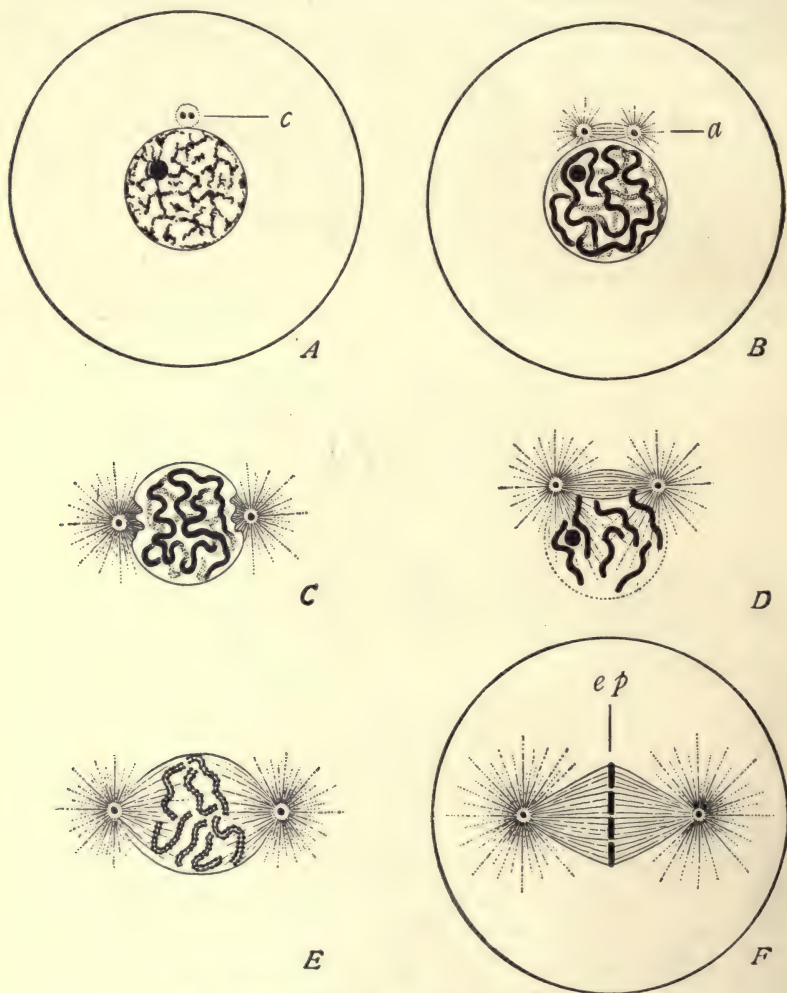


FIG. 12.—DIAGRAM OF THE PROPHASE OF MITOSIS.

a, achromatic spindle; *c*, centrosome; *e p*, equatorial plate; *A-F*, successive stages of the prophase of mitosis. (After Wilson.)

matic spindle. More frequently the asters become either partially or entirely separated from each other, after which they continue

their divergent migration until they finally reach opposite poles of the nucleus. From these points achromatic fibrils (astral rays) push into the nucleus, and, by union with their fellows of the opposite pole, form the *achromatic spindle*.

Meanwhile changes have taken place within the nucleus. The nuclear wall and nucleolus disappear, and the entire chromatin

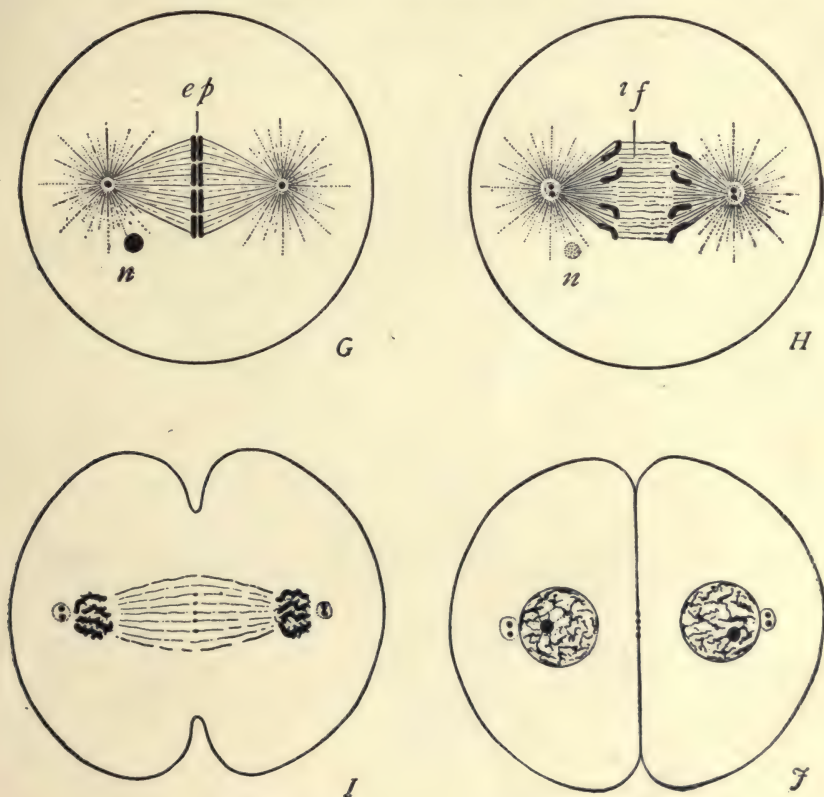


FIG. 13.—METAPHASE AND TELOPHASE OF MITOSIS.

G-H, metaphase; I-J, telophase; *ep*, equatorial plate; *if*, interzonal fibres; *n*, nebenkern. (After Wilson.)

mass, now even more intensely chromatic, unites to form a single coarse, thread-like, convoluted fiber, the chromatic *skein* or *spireme*. The spireme soon breaks into a definite number of segments or chromosomes, the number of which varies as between different animal species, but, as regards the individuals of each

species, it is fixed and unchangeable. In man the number of chromosomes is sixteen.

The termination of the prophase is marked by the approach of the chromosomes toward the equator of the achromatic spindle.

Metaphase.—The chromosomes now come to lie in the equator of the achromatic spindle, and are so arranged that each segment forms a U or V, whose apex is directed toward the axis of the spindle. When viewed from the nuclear pole, this peculiar arrange-

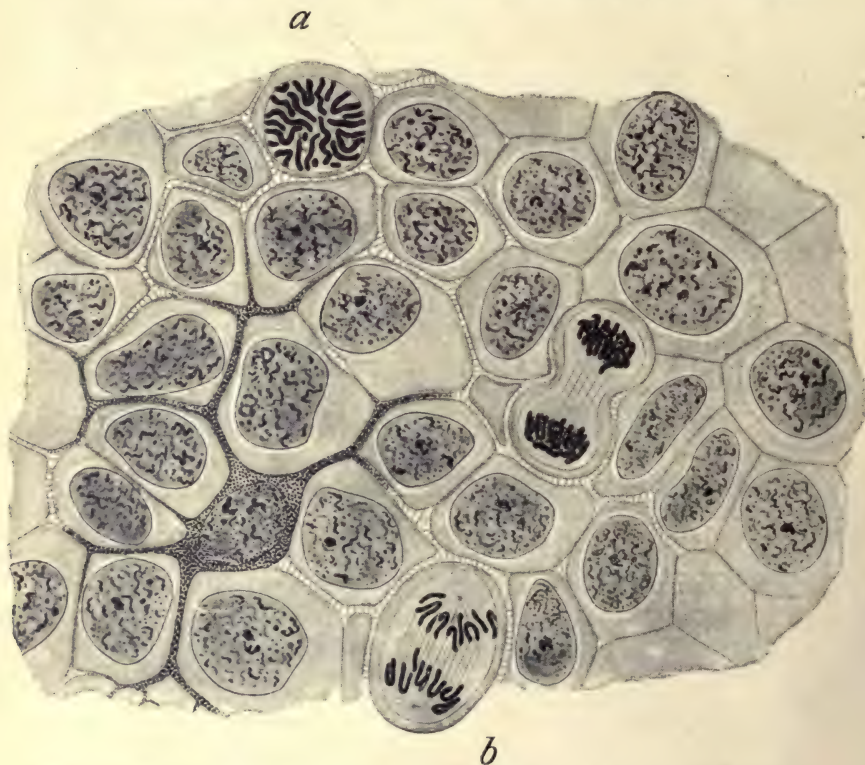


FIG. 14.—EPIDERMIS OF THE SALAMANDER. Three cells are in process of division by mitosis.

a, prophase; *b*, metaphase. The second cell above *b*, whose cell body is in process of fission, presents a stage of the telophase. (After Wilson.)

ment of the chromosomes produces a wreath-like appearance, the *monaster*.

The chromosomes now divide by longitudinal cleavage into two exactly equal portions, which promptly begin a migration

toward the opposite poles of the spindle. The two daughter nuclei thus receive from the mother cell precisely equivalent portions of chromatic substance. The cleavage of the chromatin segments frequently occurs at a very early period, and may even antedate the formation of the chromosomes by making its appearance in the spireme stage.

Anaphase.—The daughter chromosomes are now drawn toward the opposite poles of the achromatic spindle, about which they are again arranged in a wreath-like manner to form the *diaster*. The daughter chromosomes are apparently connected with each other during their migration by the fine achromatic connecting or interzonal fibers of the central spindle. Minute chromatic thickenings in the equator of this spindle (cell plate, mid-body) indicate the future plane of cytoplasmic cleavage.

Telophase.—The cytoplasm of the cell divides along the cell plate or equatorial plane of the achromatic spindle. Thus each daughter cell not only receives equivalent portions of chromatin through the daughter chromosomes, but the achromatic structures are likewise equally divided, one centrosome, with its surrounding aster or attraction sphere, going to each daughter cell. Thus a portion at least of the achromatic spindle persists as the attraction sphere of the resting nucleus. Other portions go to form the "nebenkern" which is present in many cells.

The daughter chromosomes now become thickened, convoluted, and finally crowded or fused together to form the *daughter skein* or *spireme*. The nuclear wall and nucleolus reappear, though the manner of their origin is not yet understood.

As a final change, and a preparation for future division, the centrosome frequently divides. In this case the double centrosome (diplosome) persists throughout the resting stage.

CHAPTER II

EPITHELIAL TISSUES

16

EPITHELIAL tissues, the epithelia, include all those cellular membranes which cover the free surfaces of the body, either external or internal, together with the cellular portions of the secreting glands directly connected with, or developed from, these free surfaces. They thus include the epidermis of the skin, the mucous membranes of the digestive, respiratory, and genito-urinary tracts, the cellular structures of the salivary glands, pancreas, liver, ovary, testicle, kidney, and all other glands connected with these systems. Portions of the organs of special sense—the nose, eye, and ear—are also included within the scope of the term.

The epithelial tissues are composed of cells which vary greatly in their shape and histological characters, and which may be arranged either *en masse* as in the Graafian follicles of the ovary, or in tubules or acini as in most secreting glands, or as membranes consisting of a variable number of cell layers.

These membranes are either mucous or serous. Mucous membranes include all those which are connected, directly or indirectly, with external surfaces of the body, such as those of the esophagus, stomach, bronchial tubes, bladder, etc. Their epithelium is of epiblastic origin. Serous membranes, construing the term in its broadest sense, include those cellular layers which line all of the closed cavities of the body, viz., the arachnoid membranes of the brain and spinal column, the pleuræ, pericardium, peritoneum, tunica vaginalis of the testicle, and the synovial membranes, bursæ, and sheaths of the tendons. The epithelial cells which line these latter structures, together with those forming the lining membranes of the circulatory system—heart, arteries, capillaries, veins, and lymphatic vessels—are of mesoblastic origin and are classified as *endothelium*, the term referring to their distribution *within* the closed cavities of the body. When epithelial cells are arranged to form a membrane, they may occur either as a

single layer of cells placed side by side, or the membrane may be several cells in thickness, in which case those cells upon the surface usually differ in structure and appearance from those of the deeper layers. When but a single layer of cells is present, the tissue may be called *simple* or *pavement* epithelium; when composed of several cell layers, the epithelium may be said to be complex, compound, or *stratified*.

All epithelial membranes rest upon a subjacent supporting connective tissue, the *tunica propria*, upon the free surface of which a distinct *basement membrane* or *membrana propria* is usually developed. This basement membrane is formed by fine reticular connective tissue fibers, many of which are elastic, and are flattened connective tissue cells.

In the stratified epithelial tissues the superficial cells—those nearest the free-surface—usually arise by cell division in the deeper layers, and, if they become detached by abrasion, disintegration, or by other physiological or pathological processes, they may be replaced by cell reproduction occurring in the deeper layers. When but a single layer of cells is present, as in the simple epithelial tissues, abrasion or disintegration of the cells over large areas will obviously become more difficult of replacement by cell division. Hence it is that repair of extensively destructive pathological conditions involving such epithelial tissues becomes exceedingly difficult, and often impossible.

Each epithelial cell is to some extent a secreting cell. Sometimes this is its chief function, as is the case with goblet cells, which might well be called “unicellular glands,” and which secrete an abundant supply of mucus. The same is true of those cells which form the parenchyma of secreting glands, such as the salivary glands, kidney, and liver. In many epithelia, however, secretion is a subsidiary function.

The cells of an epithelial membrane are maintained in proper juxtaposition, one to another, by means of a delicate *cement substance* which is apparently a product of their

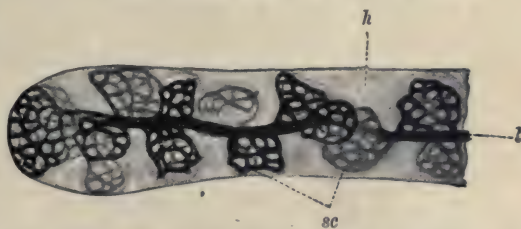


FIG. 15.—SECRETORY CAPILLARIES FROM A FUNDUS GLAND OF HUMAN STOMACH.

l, lumen of the gland; h, secreting cells; sc, secretory capillaries. (After Sobotta.)

exoplasm. This cement substance is pierced by numerous minute canals, the *secretory or nutrient canaliculi*, which are either connected with the tissue spaces of the membrana propria, or open upon the free surface of the epithelium, to which they convey the secretion of the cells. The nutrient canals occasionally are continued directly into the cytoplasm of the cell.

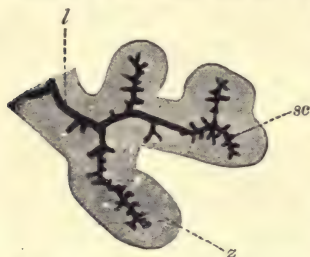


FIG. 16.—SECRETORY CAPILLARIES IN THE HUMAN PANCREAS.

l, glandular lumen; sc, secretory capillaries; z, secreting cells. (After Sobotta.) $\times 375$.

At the surface of the membrane this cement substance, from exposure to unusual mechanical and chemical influence, becomes altered in consistence, and is readily demonstrated by certain staining methods (silver nitrate, hematein, etc.). These condensed portions, when viewed from the free surface, form a network of “terminal bars,” the meshes of which are occupied by the free surfaces of the epithelial cells.

In the case of many epithelial cells—i. e., the polyhedral cells in the deeper layers of stratified epithelium, and many cells of columnar epithelium, the intercellular cement substance is bridged across by numerous fine protoplasmic threads, which, arising within the substance of one cell, become lost in the cytoplasm of its neighbors. The peculiar spinous appearance produced by these so-called *intercellular bridges* has caused such cells to be described as “prickle cells” (Fig. 8).

The intercellular bridges are more than the name implies, for they can often be traced not only from one cell to another, but may even pass entirely through an intermediate cell and enter a third or even a fourth cell. These protoplasmic processes usually follow regular curves with a convexity toward the cell nuclei, so that in passing through a cell they frequently

At the surface of the membrane this cement substance, from exposure to unusual mechanical and chemical influence, becomes altered in consistence, and is readily demonstrated by certain staining methods (silver nitrate, hematein, etc.). These condensed portions, when viewed from the free surface,

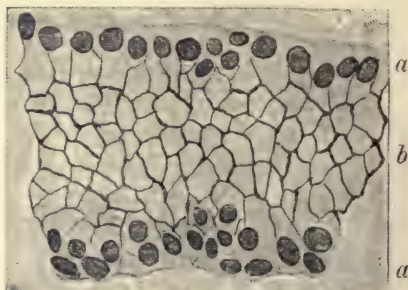


FIG. 17.—“TERMINAL BARS” OF CEMENT SUBSTANCE AS SEEN BETWEEN THE EPITHELIAL CELLS OF A TUBULAR SECRETING GLAND IN THE PYLORIC REGION OF THE HUMAN STOMACH.

The columnar epithelium is seen in profile at a; at b, the free ends of the cells are seen. Hematein. $\times 550$.

subdivide it into three or four segments, in the center of which is the nucleus. They are probably exoplasmic derivatives of the cell protoplasm. Similar fibrils, though less pronounced, have also been found in other tissues than epithelium—i. e., in smooth muscle and in nerve cells.

CLASSIFICATION OF EPITHELIA

I. **SIMPLE EPITHELIA**—those which occur *en masse*, or composing a membrane but one cell in thickness.

- | | | | |
|--|--|--|---|
| 1. Spheroidal , composed of | (a) <i>Spherical</i> cells. | <ul style="list-style-type: none"> Ovum. Cells of the Graafian follicles. Embryonal cells. Liver cells. Deeper layers of complex epithelium. | |
| | (b) <i>Polyhedral</i> cells. | | |
| 2. Squamous , composed of flattened, scaly cells. | <ul style="list-style-type: none"> (a) Lining closed cavities. <i>Pavement epithelium</i> or <i>endothelium</i>. | <ul style="list-style-type: none"> Serous membranes, synovial membranes, bursæ, and tendon sheaths; heart, arteries, capillaries, veins, and lymphatic vessels. | |
| | | | (b) Lining the alveoli of the lungs, some tubules of the kidney, the anterior chamber of the eye, and the membranes of the middle and internal ear. |
| | | | (c) As the superficial cells of stratified epithelium (<i>vide infra</i>). |
| 3. Columnar . | (A) Simple* | <ul style="list-style-type: none"> (a) Lining the mucous membrane of the alimentary tract—stomach, small intestines, large intestines. (b) Lining the ducts of all secreting glands—liver, pancreas, salivary, lachrymal, and mammary glands, testicle, prostate, etc. (c) The deepest layer of cells in stratified epithelium is composed of columnar-shaped cells, which, however, differ in structure from the true columnar type. | |
| | (B) Ciliated | | |
| | (C) Pyramidal or "glandular." | | |
| | (D) Goblet . ‡ | <ul style="list-style-type: none"> (a) <i>Respiratory tract</i>—nasal, pharyngeal, tracheal, and bronchial mucous membranes. (b) <i>Alimentary tract</i>—stomach, small and large intestines. | |
| | (E) Neuro-epithelium . | | |
| | | <ul style="list-style-type: none"> (a) <i>Eye</i>—the rod and cone cells of the retina. (b) <i>Ear</i>—in the maculæ of the labyrinth and in Corti's organ. (c) <i>Nose</i>—in the olfactory mucous membrane. (d) <i>Tongue</i>—in the taste buds. | |

II. COMPLEX EPITHELIA—those whose cells form several superimposed layers.

1. Stratified ("stratified squamous").	{ Superficial cells, <i>squamous</i> ; deeper, <i>polyhedral</i> ; the deepest, <i>columnar</i> in shape.	{ Forms the epidermis of the skin, and covers the free surface of those mucous membranes which clothe all orifices in direct connection therewith—viz., the conjunctiva and cornea; the external auditory canal; part of the nasal mucous membrane; mouth, pharynx, and esophagus; epiglottis and vocal cords; anus, as high as the internal sphincter; vagina and external por- tion of the urethra.
2. Transitional. §	{ Superficial cells only somewhat <i>flat- tened</i> ; next deeper layer, <i>pear-shaped</i> ; deepest layers, <i>polyhedral</i> .	{ Found only in the <i>urinary system</i> — viz., pelvis of the kidney, ureter, bladder, and first portion of the urethra.
3. Pseudo-strati- fied columnar.	{ Superficial cells, <i>co- lumnar</i> ; † deeper cells, <i>polyhedral</i> or <i>spindle-shaped</i> . (a) <i>Non-ciliated</i> (rare). (b) <i>Ciliated</i> .	{ (a) Part of vas deferens. (b) Respiratory tract; nasal mucous membrane and passages connected therewith, tear-ducts, Eustachian tube, etc., larynx, trachea, and bronchi. Genital tract; epididymis and vas deferens.

* Usually designated "columnar" by way of abbreviation. Short columnar cells are often called "*cubical*," or "*cuboidal*," and are included under this head.

† In later life these cells lose their cilia.

‡ Cells whose protoplasm has been converted into mucinogen. They may be considered unicellular, mucus-secreting glands.

§ Differentiation of this variety of epithelial tissue, though neglected by some authors, becomes most important in the clinical examination of urine where it is necessary to determine the origin of individual cells. Transitional cells from the bladder are easily distinguished from the stratified cells of the vagina, urethra, or epidermis.

|| The "superficial" cells of this variety extend throughout the entire thickness of the membrane. Hence this form of epithelium may in one sense be called "simple" rather than "stratified."

SPHEROIDAL EPITHELIUM.—In their early embryological condition all epithelial cells are nearly spherical in shape, but, apparently from pressure during growth or development, or from other unknown causes, they are distorted according to the direction of the pressure applied, and according to the number of points of application. Pressure unequally applied on many sides naturally produces a polyhedral shape.

Such is the condition of the epithelial cells which compose the parenchyma of the liver. The liver cell may therefore be considered as exhibiting the typical structure of spheroidal epithelium. These cells are polyhedral in shape; in profile, polygonal. They consist of soft, finely granular protoplasm, whose surface is slightly condensed to form an indistinct limiting membrane. Within the cell a distinct spherical nucleus—sometimes two nuclei—may be observed. The nucleus is deeply chromatic. Small fat globules or vacuoles, pigment, and secretory granules (zymogen, glycogen, etc.) are found within the cytoplasm. Such cells are often surrounded by a network of lymphatic spaces, nutrient canals, or secretory canaliculi, and from these minute canals, still finer offshoots penetrate the cytoplasm of the cell.

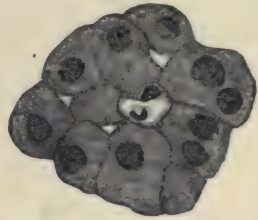


FIG. 18.—POLYHEDRAL EPITHELIUM, FROM A SECTION OF THE HUMAN LIVER.

The central blood capillary contains one leucocyte, and its wall contains the nucleus of a flattened endothelial cell. Hematein and eosin. $\times 550$.

SQUAMOUS EPITHELIUM (*pavement epithelium*).—The cells of this variety vary much, according to their location. Those lying within the body (endothelium) are of soft consistence, highly elastic, and form minute plate-like masses of protoplasm, joined edge to edge by cement substance, to form a continuous yet extremely thin membrane. Within each cell is a large oval nucleus, which, like the cell body, is much flattened. The nucleus, however, forms the thickest portion of the cell, and is usually found near its center.

In those cells which are exposed upon the free surface of the body, such as the superficial cells of the epidermis or of the mucous membrane of the mouth or pharynx, the cell cytoplasm becomes changed in consistence as it changes its relative position in the cell layer. A peculiar horny material, known as “keratin,” is developed within the superficial squamous cells of stratified epithelium, which obscures their nucleus and changes the cell protoplasm into a firm horny substance. By the action of alkalis, such cells may be softened and the nucleus again brought into view. These cells, when seen “on the flat”—their broad surfaces presenting—are irregularly polygonal in outline, and have serrated margins and sharp angles. When viewed in profile, however—viz., their edges presenting—as frequently occurs in transections

of endothelial membranes, squamous epithelial cells appear either as mere lines or as spindle-shaped bodies whose bulging center incloses the flattened nucleus.

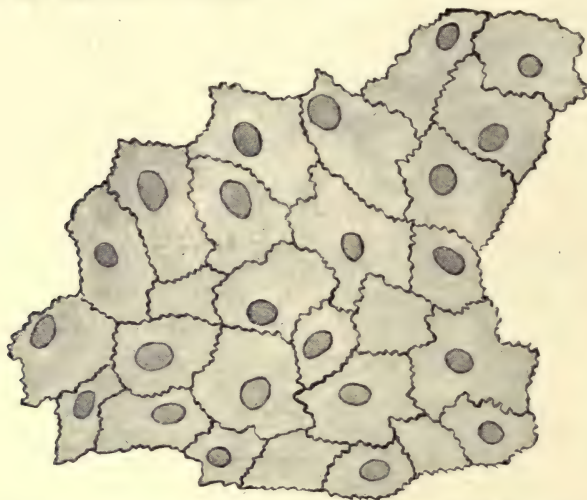


FIG. 19.—SQUAMOUS EPITHELIUM OR ENDOTHELIUM (surface view).

From the mesentery of a rat. Silver nitrate and hematein. $\times 550$.

SIMPLE COLUMNAR EPITHELIUM.—Simple columnar cells occur as cylindrical bodies of varying length. Their deeper or attached extremity often tapers nearly to a point, and is frequently bifid. A surface view of a membrane consisting of columnar cells shows the free extremity of each cell to be of polygonal outline, the cells collectively forming a beautiful mosaic (Fig. 17). Each cell consists of finely granular cytoplasm and contains an oval nucleus, the long axis of which corresponds with that of its cell. The free extremity of these cells has frequently a peculiarly fine striated border, the *cuticular margin*; it is distinguished from the body of the cell by a very delicate membrane. When present, this peculiar striated border or *cuticle* is characteristic of the columnar type of cell, and is specially typical of those columnar cells which occur in the digestive tract.



FIG. 20.—COLUMNAR EPITHELIUM FROM THE PYLORIC REGION OF THE HUMAN STOMACH. (Profile view.)

Hematein and eosin. $\times 550$.

The attached extremity of the columnar epithelial cells frequently presents a longitudinally striated appearance. Such "*rodged epithelium*" is specially characteristic of the ducts of the salivary glands and pancreas, and of certain of the uriniferous tubules of the kidney.

Short columnar cells, those whose three axes are approximately equal, are frequently described as *cubical* or *cuboidal epithelium*, but these cells do not differ either in structure or in distribution from the ordinary columnar type.

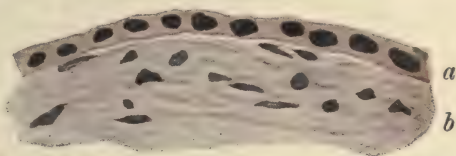


FIG. 21.—CUBOIDAL EPITHELIUM FROM THE RETE TESTIS OF THE RABBIT.

a, epithelium; b, connective tissue. Hematein and eosin. $\times 550$.

CILIATED CELLS.—Many cells carry upon their free surface a group of delicate hair-like processes called *cilia*, or a single *flagellum*, which during life are capable of a rapid vibratory or undulating motion. The direction of this ciliary motion is constant, and is such as to produce a definite current within the fluids which bathe the surface of these cells, whose direction is invariably from within outward—viz., toward the external surface of the body. In the human body cilia occur almost exclusively upon the free extremities of columnar-shaped cells. In some of the lower animals, as, for example, in the mouth of the frog, cilia are also found upon polyhedral or pear-shaped cells. The cilia are evidently extensions of the cytoplasm of the cell body, and may be regarded as modifications of its exoplasm.

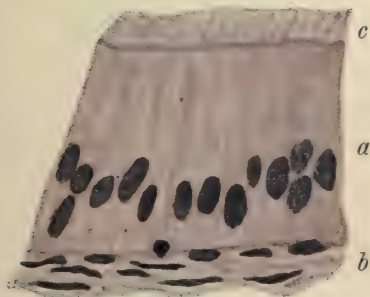


FIG. 22.—COLUMNAR CILIATED EPITHELIUM FROM THE EPIDIDYMIS OF A RABBIT.

a, epithelium; b, connective tissue; c, cilia. A leucocyte is seen between the bases of the columnar cells. Hematein and eosin. $\times 550$.

The ciliated cell border is differentiated from the protoplasm of the cell body by a fine chromatic line which is divisible into a number of knob-like segments. The cytoplasm and nucleus of ciliated epithelium, except for the peculiarities dependent upon

The ciliated cell border is differentiated from the protoplasm of the cell body by a fine chromatic line which is divisible into a number of knob-like segments. The cytoplasm and nucleus of ciliated epithelium, except for the peculiarities dependent upon

the formation of cilia, is similar to that of the simple non-ciliated columnar cells. Their cytoplasm, as in other types, may contain vacuoles, pigment granules, paraplast, and even secretory granules.

PYRAMIDAL CELLS—"GLANDULAR EPITHELIUM."—This variety of the columnar cell occurs in the secreting glands. It is, perhaps, unnecessary to distinguish it from the simple columnar cell, there being but little difference in the structure of their protoplasm. The peculiar shape which characterizes these cells results from their disposition to form the wall of secreting tubules, sacular acini, etc. The greater area of their base as compared with that of their free extremity gives them the shape of a truncated pyramid. A cuticular border is not usually present. The cells are partially or completely loaded with secretory granules.

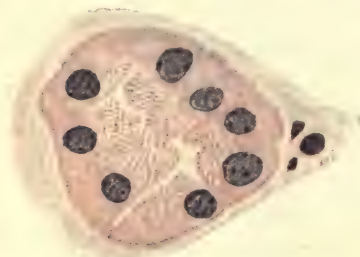


FIG. 23.—A GROUP OF CELLS FROM A TRANSECTION OF AN ACINUS OF THE HUMAN PANCREAS; GLANDULAR EPITHELIUM.

Hematein and eosin. $\times 550$.

Pyramidal or glandular epithelium is found in tubules of the kidney, salivary glands, and pancreas, in the secreting glands of the gastric and intestinal mucous membrane, in the mucous glands of the esophagus, pharynx, bronchial tubes, and oral and nasal cavities, and in the secreting glands of the skin.

GOBLET CELLS.—These cells are derivatives of the columnar variety, and may occur among either the plain or ciliated columnar cells. Goblet cells are most abundant in the intestinal tract, but are also to be found in the stomach, bronchial tubes, trachea, nasal mucous membrane, and in the ducts and tubules of mucus-secreting glands. In such epithelial membranes certain columnar cells, if not indeed all of these cells, are destined to secrete mucus. The cytoplasm of such cells is converted into a clear, poorly chromatic mass of a peculiar glassy or vitreous appearance, which occupies an increasing proportion of the free extremity of the cell. This "*mucinogen*," when acted upon by alcohol, is precipitated within the cell, and then forms fine basophile fibrils or granules, which stain deeply with the muchematein and mucicarmine solutions of P. Mayer. At the base of the goblet cell its nucleus is embedded in a minute mass of unaltered granular cyto-

plasm and is often flattened against the basement membrane, the amount of flattening being proportionate to the volume of its mucous content.

The accumulation of mucinogen within its cytoplasm expands the cell, finally ruptures its wall in the direction of least resistance, and thus permits its mucous content to exude upon the free surface, leaving behind the small granular protoplasmic cell remnant attached to the basement membrane. The further history of these cell remnants is somewhat doubtful. They are possibly absorbed, removed, and finally replaced by mitotic division of adjacent cells. There is, however, some evidence to show that they are still



FIG. 24.—GOBLET CELLS AS SEEN IN A TRANSECTION OF A CRYPT OF THE LARGE INTESTINE OF MAN.

Sections of five goblet cells are seen among the columnar cells which line the tubule. Muchematein and eosin. $\times 550$.

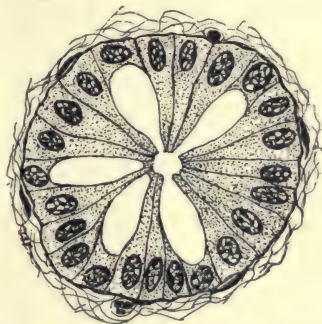


FIG. 25.—DIAGRAM SHOWING THE ARRANGEMENT OF THE COLUMNAR AND GOBLET CELLS OF THE PRECEDING FIGURE.

The goblet cells are represented as being empty; their unaltered basal portions containing the nucleus are distinctly seen.

capable of further growth, whereby they may regain their original form and become again capable of passing through the same stages of secretory activity.

NEURO-EPITHELIAL CELLS.—These cells are derivatives of columnar epithelium which are specially differentiated to form nerve end-organs. They are usually elongated cells having a bulging nucleated center, their free extremity either projecting beyond the epithelial surface as a bundle of fine cilia or as a slender non-ciliated process which terminates within a pore-like opening directly connected with the free surface. Their attached extremity, tapering to a fine process, is in relation with the terminal arborization of the axis cylinder of a nerve fibre. Neuro-epithelium is found only in the several organs of special

sense, and will be more fully described as a part of these several organs.*

STRATIFIED EPITHELIUM.—This variety of epithelium occurs as a membrane of varying thickness but always comprising several cell layers. A straight line perpendicular to its free surface would penetrate from five to thirty or more epithelial cells. But while there is a wide diversity in the thickness of the epithelial layers, the character of the cells at any given level is very nearly constant. Thus the deeper cells, those nearest the basement membrane, are nucleated, of soft consistence, and may contain mitotic figures, indicating that it is at this level that cell reproduction is most active. Toward the surface of the membrane the cells become progressively of firmer consistence, so that the most superficial ones present a horny appearance as a result of the gradual keratization of the cytoplasm during the progress of the cell toward the surface. The keratization is apparently dependent upon surrounding mechanical conditions, for it is much more marked in the skin, which from constant and rapid evaporation is comparatively dry, than in the mouth, esophagus, or conjunctiva, where the epithelium is constantly moistened by glandular secretions: the margins of the lips, eyelids, etc., present an intermediate state of keratization.

With these chemical changes in the composition of the cytoplasm there are corresponding changes in its nucleus. In the deeper cells, the nucleus is oval or spherical and highly chromatic. Toward the surface, the nucleus becomes more and more flattened and more and more obscured by the cornification of the cell protoplasm. In the most superficial cells it is usually impossible to demonstrate the nuclei, except by acting upon their protoplasm with strong reagents such as the caustic alkalis, soda or potassa.

But the most characteristic change in the cells of stratified epithelium is the progressive transition in shape during their passage from the deeper layers to the free surface. New cells, resulting from indirect division of the cells in the deeper layers, are, by continued reproduction, gradually pushed toward the surface, whence they are constantly being desquamated in small scaly masses. The pressure exerted in this process tends to gradually flatten these cells so that their vertical diameter, that perpendicular to the surface, becomes progressively shorter the nearer they

* See chapters on the Eye, the Ear, the Olfactory Organ, the Tongue, and on Nerve End-organs.

approach the free surface; on the other hand, their transverse diameter, that parallel to the surface of the epithelial membrane, is correspondingly increased. The deepest cells of stratified epithelium—those which rest upon the basement membrane—are elongated in their vertical diameter, and possess an irregularly columnar shape.* Their nuclei are likewise elongated, oval or

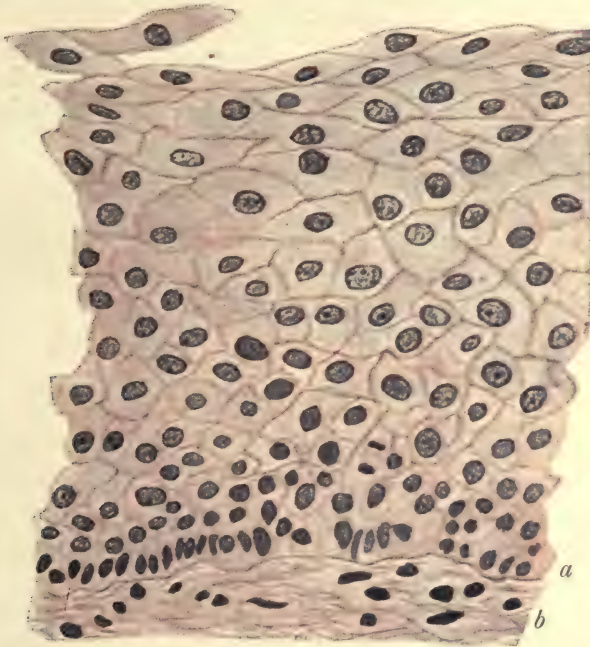


FIG. 26.—STRATIFIED EPITHELIUM FROM THE HUMAN ESOPHAGUS.
a, basement membrane; b, connective tissue. Hematein and eosin. $\times 410$.

elliptical in shape. Superficial to these, but still in the deeper layers, are polyhedral cells with spherical nuclei, which are known as *prickle cells* because of their prominent intercellular bridges. Superficial to the prickle cells, the epithelial cells become progressively more flattened, until at the surface they are mere scales. This gradual transition from columnar and polyhedral cells below,

* In the skin of brunettes and the dark-skinned races, and in the epithelium of the skin of the scrotum, peri-anal region, and areolæ of the breasts, these cells contain small granules of the pigment to which the color of the cuticle is due. This columnar cell layer is then described as the layer of pigment epithelium.

to thin flat scales on the surface is characteristic of all stratified epithelium.

The thin superficial scales resemble very closely in shape and appearance the squamous epithelium previously described. The

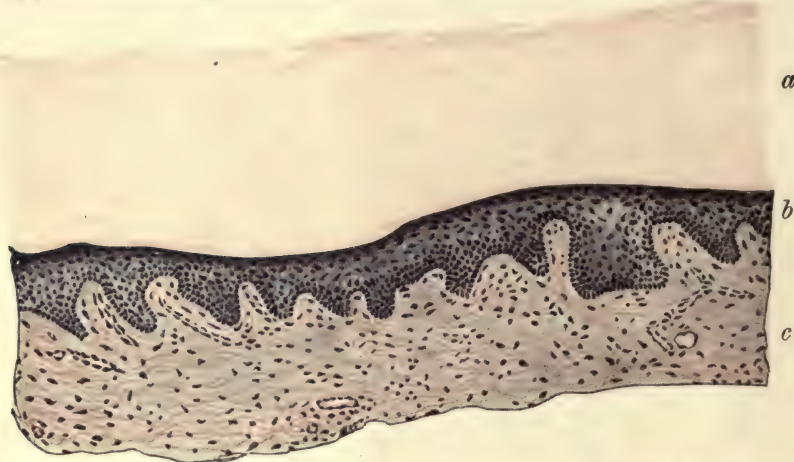


FIG. 27.—EPIDERMIS OF THE SKIN OF THE FINGER TIP, SHOWING EXTREME KERATIZATION OF THE EPITHELIUM.

a, keratized epithelium; *b*, Malpighian or germinal layer; *c*, connective tissue.
Hematein and eosin. $\times 50$.

deeper cells have a finely granular cytoplasm and distinct nuclei except when obscured by the appearance of keratin within their protoplasm. Many of these cells contain coarse granules of *eleidin* and *keratohyalin*—substances chemically intermediate between the unaltered and the keratized protoplasm.

As stated, the formation of *keratin* within these cells is more active in those membranes which are comparatively dry from exposure to the air. Consequently, it is most active in the epidermis of the skin. If stratified epithelium is at all times well moistened, as, for example, in the mouth and esophagus, the formation of keratin is slight, and the soft polyhedral cells compose the major portion of the epithelial membrane which then has only a thin superficial covering of flattened scaly cells. In the comparatively dry epidermis, on the other hand, the flattened horny cells frequently occupy more than half the thickness of the epithelial layer. In the superficial squamous cells of moist membranes the nucleus can always be readily demonstrated, even in the keratized cells of the extreme surface.

TRANSITIONAL EPITHELIUM.—This variety of epithelium resembles the preceding, in that it is composed of several cell layers, the deeper cells of which are more nearly polyhedral but are somewhat flattened upon the free surface. It differs, however, in the number of cell layers, which is much less than is usual in the preceding variety, and in the character of the superficial cells. Transitional epithelium is not usually more than from three to ten cells deep, four to six being the rule. The numerical as well as the actual thickness of epithelial membranes is to a certain extent dependent upon their state of tension during life; thus the transitional epithelium of the urinary bladder is much thicker when the organ is collapsed than during distention.



FIG. 28.—TRANSITIONAL EPITHELIUM FROM A TRANSECTION OF THE URETER OF AN INFANT.

a, epithelium; *b*, connective tissue. Hematein and eosin. $\times 550$.

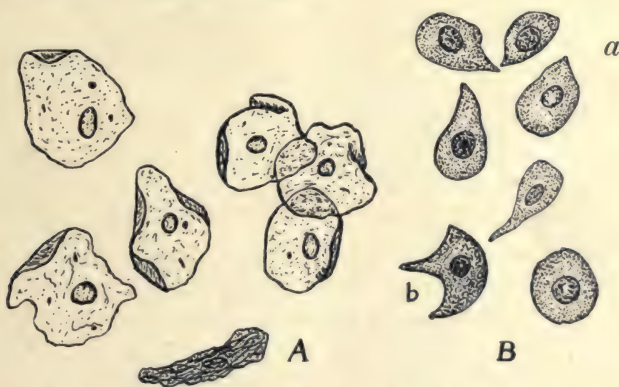


FIG. 29.—ISOLATED CELLS OF THE HUMAN URINE.

A, from the vagina of a woman (stratified squamous epithelium); *B*, from the ureter of a child (transitional epithelium); *a*, cells from the deep layers; *b*, superficial cell. Moderately magnified.

The deepest cells are polyhedral, and these form the greater portion of the membrane. Only the more superficial layers differ therefrom. Those polyhedral cells which lie in the mid-region of the epithelial layer possess a peculiar flask or pear-shape, with well-rounded bodies and a broad tapering process which is embedded between the adjacent cells of the deeper layers. The rounded extremities of the pear-shaped cells fit into peculiar indentations in the deeper surface of the superficial layer of epithelial cells, producing peculiar concave facets, which are particularly characteristic of the detached superficial cells of transitional epithelium.

The superficial cells, while somewhat flattened, usually have a thickness equal to one-sixth to one-third their transverse diameter. In this respect they differ markedly from the superficial scaly cells



FIG. 30.—PSEUDO-STRATIFIED COLUMNAR CILIATED EPITHELIUM FROM A BRONCHIAL TUBE OF MAN.

a, a goblet cell; *b*, cilia; *c*, superficial cytoplasmic layer; *d*, deeper nucleated layer, the nuclei of the columnar cells are somewhat more deeply stained than those of the basal cells; *e*, basement membrane; *f*, connective tissue. Hematein and eosin. $\times 550$.

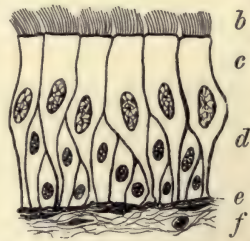


FIG. 31.—DIAGRAM SHOWING THE MANNER IN WHICH ALL THE EPITHELIAL CELLS OF PSEUDO-STRATIFIED CILIATED EPITHELIUM REACH THE BASEMENT MEMBRANE.

Letters as in the preceding figure.

of stratified epithelium and are easily distinguished therefrom, even in the isolated condition in which they are frequently found in the urine. The concave facets on their under surface, as well as the peculiar pear-shape and small size of the deeper cells, are sufficient to distinguish the transitional cells from those of stratified epithelium.

There is little, if any, formation of keratin in transitional epithelium. This is possibly explained by the fact that, as it occurs

only in the urinary system, this form of epithelium is always well moistened.

PSEUDO-STRATIFIED COLUMNAR EPITHELIUM.—The superficial cells only of this variety of epithelium are columnar in shape, and except in one or two unimportant places are always ciliated. The deeper extremities of these columnar cells taper to a point, and extend all the way to the basement membrane. Between the tapering ends of these cells small spindle-shaped and spheroidal cells are closely packed. The several varieties of cells thus appear to be superimposed, though all actually rest upon the basement membrane. The distribution of this variety of the epithelium is practically identical with that of ciliated cells. The deeper extremities of the columnar cells are occasionally bifid or even somewhat varicose in order the more closely to fit between the spindle-shaped and spheroidal cells of the deeper portion. The nucleus of these latter cells is usually situated a little below the middle of the columnar cell, so that all the nuclei of the epithelial membrane lie within its deeper half, thus giving to this portion a more deeply chromatic appearance when observed in stained sections under low magnification. The superficial half of the epithelial layer contains only the cytoplasmic portion of the columnar cells with their ciliated borders.

CHAPTER III

CONNECTIVE TISSUES

WHILE in the epithelial tissues the cells are chiefly developed at the expense of the intercellular elements, in the connective tissues the conditions are the reverse. The intercellular elements are here developed out of all proportion to the connective tissue cells. The cells of these tissues, therefore, are scanty, the ground substance considerable, and within the latter a new element, the connective tissue fibre, makes its appearance. The fibres are of three varieties: *white connective tissue fibres*, *yellow elastic fibres*, and *reticulum*. In any given location either of these varieties may predominate to such an extent as to determine the character of the mature tissue, while in the immature forms of connective tissue it is the cellular elements which attain the greatest prominence.

The minute structure of connective tissue is subject to great and important changes during its development. Beginning, as it

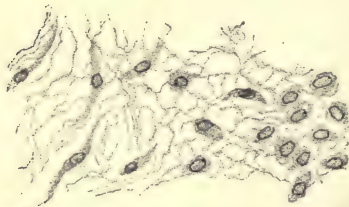


FIG. 32.—EMBRYONIC CONNECTIVE TISSUE, EARLY STAGE. Highly magnified.
(After Mall.)

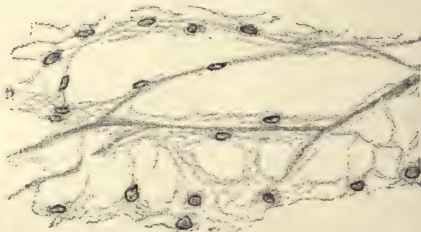


FIG. 33.—EMBRYONIC CONNECTIVE TISSUE AT A LATER STAGE THAN IS REPRESENTED IN FIG. 32. (After Mall.)

does, with the primitive mesoblast, connective tissue is originally a cellular structure. The mesoblastic germ cells of connective tissue not only increase in number, by cell division but also secrete an intercellular ground substance of semifluid consistence. The

mesodermic cells, according to Studnička,* by fusion with each other finally form a syncytial tissue, in which there promptly occurs a differentiation of the cytoplasm with the formation of an endoplasm and an exoplasm, and within the latter the fine fibrils



FIG. 34.—AREOLAR CONNECTIVE TISSUE OF THE MATURE TYPE, FROM THE REGION OF THE KIDNEY OF MAN.

a, fat cells, the one at *a'* is so cut as to show the surface of the spheroidal cell (the fat has been removed); *b*, connective tissue cells of the lamellar type; *c*, coarse bundle of white fibres; *d*, elastic fibres, most of them very obliquely cut. Hematein, picro-acid fuchsin, and Weigert's elastic tissue stain. $\times 750$.

soon make their appearance. This process progresses, new ground substance and fibres being constantly formed at the expense of the endoplasm, until finally the latter again forms isolated cells.

* Anat. Anz., 1903.

The culmination of these changes results in the mature fibrillar connective tissue in which the cells are shrunk and scarce, though still apparently capable of assuming renewed activity when occasion requires.

Embryonic connective tissue is therefore typically cellular as compared with the mature type; its ground substance is abundant, but the fibres, whose development is as yet incomplete, are scanty. Such embryonic connective tissue is found not only in the fetus, but also in early childhood, and in the adult especially during regeneration of destroyed areas of connective tissue, and in other more or less pathological conditions.

Connective Tissue Cells.—Connective tissue cells not only vary in number as they approach maturity, but in their structure and appearance as well. The cells of embryonic connective tissue are comparatively large, are frequently stellate from the presence of numerous interlacing and sometimes anastomosing branches, and their cytoplasm has a typical reticular or granular appearance. In the later stages of their development ameboid motion has been observed in such cells, and, within the limits of the tissue in which they are developed, they are presumably endowed with the power of locomotion.

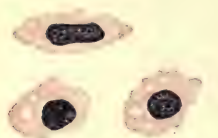


FIG. 35.—PLASMA CELLS
OF CONNECTIVE TIS-
SUE FROM THE HU-
MAN BREAST.

Hematein and eosin.
× 750.

In the neighborhood of developing blood-vessels *plasma cells* of large size and irregular shape are frequently seen. The cytoplasm of these cells is of considerable volume, and is prolonged into broad protoplasmic branches of considerable length. Both in the cell body and in the processes vacuoles are so numerous as to give the cell a typically reticular appearance, a peculiarity which is emphasized by the removal of the contents of the vacuoles, as frequently happens in the preparation of microscopical specimens.



FIG. 36.—SPINDLE-SHAPED CON-
NECTIVE TISSUE CELLS FROM
THE STROMA OF THE HUMAN
OVARY.

Hematein and eosin. × 550.

In the denser forms of mature connective tissue, where the cells are apparently subjected to more or less compression between the firm bundles of fibres, the connective tissue cells lose their typical embryonal stellate form and become somewhat fusiform; they are then known as the *spindle cells* of connective tissue. Such

cells occur in great abundance in the stroma of the ovary and the mucosa of the uterus and oviduct.

In the mature tissue of the adult many of the cells become more or less flattened, and are often closely applied to, or even wrapped around, the fibre bundles. These *lamellar cells* have a small nucleus, a considerable rim of cytoplasm, which frequently has a shrunken appearance, and sometimes a few short cytoplasmic processes. The branching stellate forms, however, are characteristic of the younger connective tissues.

In certain locations a deposit of pigment granules occurs within the connective tissue cells. Such *pigment cells* are usually found where protection from light seems desirable, and are most abundant in the choroid coat and iris of the eye. The pigment granules are entirely confined to the cytoplasm of the cell; the nucleus is never invaded by the deposit.

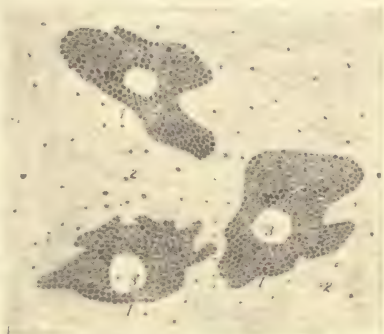


FIG. 37.—PIGMENTED CELLS FROM THE CHOROID COAT OF THE OX'S EYE. (Unstained; hence, only the pigment granules appear in the figure.)

1, granules contained within the cytoplasm; 2, free granules which have escaped from cells injured during the process of teasing; 3, the non-pigmented nuclei.

The cytoplasm of certain connective tissue cells contains coarse basophile granules, which stain with dahlia and similar basic dyes.

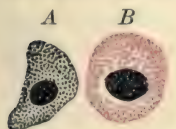


FIG. 38.—GRANULE CELLS FROM THE FIBROUS CONNECTIVE TISSUE OF THE HUMAN MAMMARY GLAND.

A, a basophile cell; B, an eosinophile cell. Hematein and eosin. $\times 750$.

This type is known as *granule cells*, or Mast cells (*Mastzellen* of the German authors). The granules of other granule cells are readily stained with acid dyes, such as eosin (*eosinophile* or *acidophile* granule cells). According to the observations of H. B. Shaw,* certain of the granule cells abound in those locations where fat is deposited, and have a special relation to the development of the *fat cells* of adipose tissue.

All the forms of connective tissue cells so far enumerated have their origin within the tissue area in which they lie, hence they are termed

* J. Anat. and Physiol., 1901.

fixed or *histogenic connective tissue cells* in contra-distinction to the leucocytes which wander out from the blood into the tissue spaces of the connective tissues, and which are then called the *wandering* or *hematogenic connective tissue cells*. These latter cells may present the same varieties as the white blood cells from which they are derived.

The several varieties of **connective tissue cells** may be classified as follows :

- | | | |
|-------------------------------|---|-------------------------------|
| I. HISTOGENIC OR FIXED. | { | (a) Lamellar cells. |
| | { | (b) Spindle cells. |
| | { | (c) Plasma cells. |
| | { | (d) Granule cells. |
| | { | (e) Fat cells. |
| | { | (f) Pigment cells. |
| | { | (g) Embryonic stellate cells. |
| II. HEMATOGENIC OR WANDERING. | { | (h) Leucocytes. |

Types of Connective Tissue.—The proportions and character of the cells and fibres present in any given connective tissue, to a certain extent, determine its character. If the white fibres of connective tissue are closely packed in dense parallel bundles, the elastic fibres being comparatively insignificant in number, the type of connective tissue may then be said to be dense fibrous or white fibrous tissue.

In elastic tissue, on the other hand, the yellow elastic fibres are highly developed, the white fibres forming only insignificant and very delicate sheaths, which inclose the coarser elastic fibres.

Again, it is the variety of delicate connective tissue fibre known as reticulum which preponderates in reticular tissue, and if the meshes of this reticular network become infiltrated by leucocytes, which then multiply by division until they exceed the other tissue elements, the connective tissue is then said to be of the lymphoid or adenoid variety. In all we distinguish the following **varieties of connective tissue**: 1, embryonic; 2, gelatinous; 3, areolar; 4, dense white fibrous; 5, elastic; 6, adipose; 7, reticular; 8, lymphoid.

Embryonic connective tissue (Figs. 32 and 33) occurs not only in fetal and infantile life, but also during the regeneration of destroyed connective tissue areas and in pathological neoplasms. It is distinctly cellular in character. Its cells are spindle-shaped and stellate, are much branched, and, through their larger processes, they frequently anastomose.

The fibres are extremely fine; they are not usually arranged in bundles, but form a delicate network which permeates the ground substance in every direction. In the very immature types the fibres are all of the white fibrous variety; fine elastic fibres appear later. The fluid ground substance forms an abundant mass of tissue juice which occupies the meshes of the fibrous net.

Gelatinous connective tissue (mucous or mucoid connective tissue) occurs only in the umbilical cord, where it forms the "jelly of Wharton," and in the vitreous humor of the eye. Its semifluid

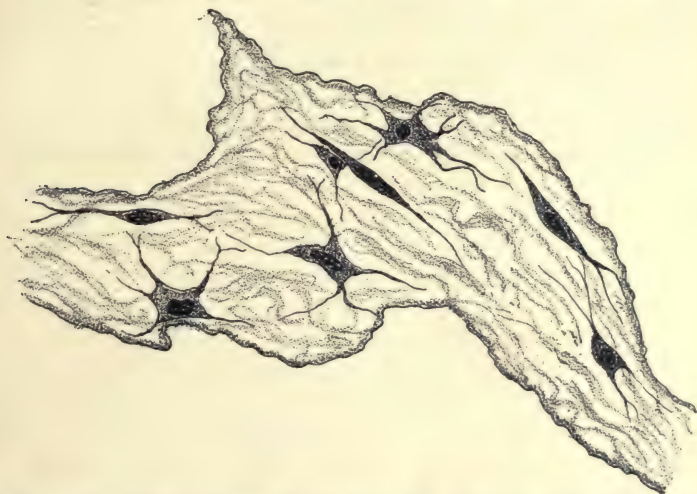


FIG. 39.—GELATINOUS CONNECTIVE TISSUE FROM THE UMBILICAL CORD OF A NEW-BORN INFANT.

Safranin and water blue. $\times 410$.

ground substance is of a gelatinous consistence, and forms the greater portion of the tissue; in the vitreous humor there is little else.

The cells are mostly of the branched lamellar variety, are few in number in the vitreous, but more abundant in the umbilical cord. In the vitreous humor, also, there are very few fibres; those which are present are very fine, and form a delicate reticulum. In the umbilical cord the fibres are more abundant, and possess a tendency to form bundles, which are disposed in parallel cylindrical layers around the large blood vessels.

Areolar connective tissue (Fig. 34) is the most widely distributed of all the varieties; it fills all otherwise unoccupied spaces within

the body, and in all microscopical sections areolar tissue is almost invariably to be found. This tissue connects the skin with the underlying structures, maintains the position and relation of adjoining muscles, surrounds the heart and its great vessels, envelops the abdominal viscera, occupies the spaces of the mediastinum, and fills similar intervals between the various organs in all parts of the body.

The *ground substance* of areolar tissue is a coagulable fluid, the *tissue juice*. Solutions of silver nitrate injected into the interstices of areolar tissue coagulate its tissue juice or ground substance and darken it slightly. It is then seen to be permeated by broad lymphatic channels, which are lined by delicate endothelial cells (W. G. MacCallum *).

Both white fibrous and yellow elastic fibres occur in areolar tissue, the former being far in excess of the latter. The comparatively loose reticular arrangement of the fibres of areolar tissue affords a most favorable opportunity for the study of these connective tissue elements.

The *white fibres* in mature tissues are invariably arranged in bundles which interlace with one another to form an open network. Each bundle consists of a number of very fine fibres, whose course is characteristically wavy or undulating. Though the individual fibres rarely branch, the fibre bundles frequently anastomose with one another. The white fibres are readily stained with most "acid" dyes, and possess a special affinity for acid fuchsin. On boiling they yield gelatin, and are readily dissolved by boiling in dilute acids or alkalis; they are digested by artificial gastric juice in five or ten minutes, but are scarcely altered after several hours when acted upon by solutions of pancreatin. After boiling, however, white fibres are readily digested by pancreatin.

The *elastic fibres* of areolar tissue, in comparison with the white fibres, are few in number. They occur as isolated fibres—never in bundles—which frequently branch and anastomose, forming in this way a very fine net with wide meshes, within which are the interlacing bundles of white fibres. The elastic fibres exist under a certain tension during life, so that their course, under favorable conditions, is invariably straight. When areolar tissue is removed from the body this tension is frequently relieved, and the elastic fibres then curl up, especially at their free ends. Under these

* Arch. f. Anat., 1902; also Bul. J. Hop. Hosp., 1903.

conditions they are no longer straight, but present a gracefully curved contour. The elastic fibres also possess a glassy, shining, or highly refractive appearance, the white fibres by comparison looking dull and opaque.

Elastic fibres stain but slightly with most dyes; they are readily colored by orcein and by Weigert's elastic tissue stain, both of which serve as specific dyes for these fibres. Elastic fibres are not dissolved by dilute acids or alkalis, even when boiled, and are only digested by artificial gastric juice after a lapse of several hours; they are, however, readily digested in faintly alkaline solutions of pancreatin.

The *cells* of areolar tissue are few in number, but may include any of the several varieties, though lamellar and spindle cells together with leucocytes form the more common types. Many of the lamellar cells are closely applied to, or even wrapped around

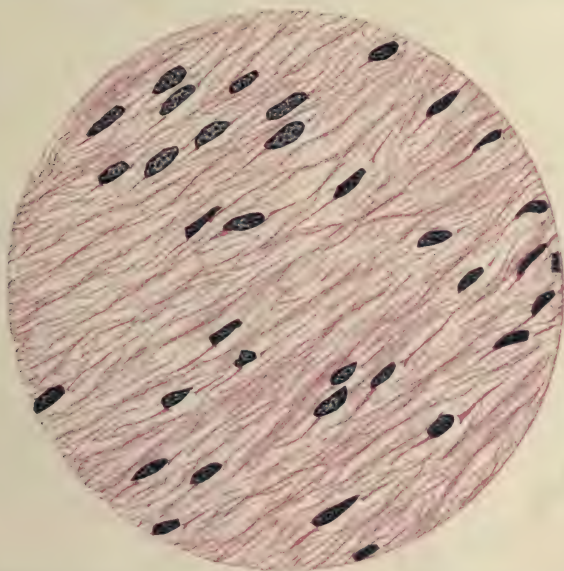


FIG. 40.—DENSE FIBROUS TISSUE FROM THE TENDON OF ONE OF THE OCULAR MUSCLES OF A CHILD.

Hematein and eosin. $\times 550$.

the bundles of white fibres. Fat cells occur in considerable numbers in all areolar tissue and in some places are aggregated into large groups which form lobules of fatty tissue.

Dense White Fibrous Tissue.—In dense fibrous tissue the ground substance is comparatively deficient. Large bundles of white fibres are arranged in approximately parallel rows, and are so closely packed as to form a dense, firm, highly resistant tissue. Its scanty connective tissue cells are of the lamellar variety and are usually arranged in rows which occupy the interstices between the parallel fibre bundles.

Dense white fibrous tissue occurs in tendons; in these the connective tissue cells often have a peculiar quadrate shape and are arranged in rows of exceptional regularity. It also forms the ligaments, the fasciæ, the muscular sheaths, and the enveloping capsules of many of the viscera. Thus it surrounds the liver, kidney, lymphatic nodes, and other organs; it also forms the valves of the heart, the tendinous rings which surround the cardiac orifices, and the chordæ tendinæ which are attached to its valves; and, in general, it is found wherever great firmness and resistance are required.

Elastic fibres in this tissue are relatively few in number and are so obscured by the dense bundles of white fibres as to be scarcely demonstrable except by means of the specific stains.

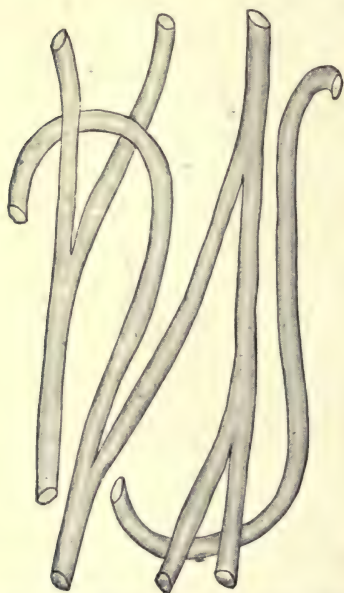


FIG. 41.—COARSE ELASTIC FIBRES FROM THE LIGAMENTUM NUCHÆ OF THE OX; ISOLATED BY TEASING.

Partly diagrammatic. \times about 250.

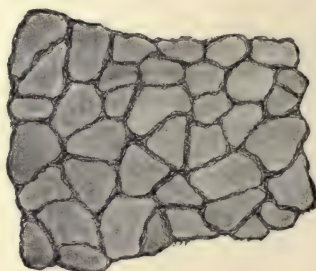


FIG. 42.—TRANSECTION OF A FASCICULUS OF THE LIGAMENTUM NUCHÆ OF THE OX, SHOWING THE VERY LARGE ELASTIC FIBRES EMBEDDED IN A VERY DELICATE NETWORK OF WHITE FIBRES.

Picro-fuchsin. \times 550.

Elastic Tissue.—In this form of tissue the elastic fibres are developed at the expense of the white fibres. The ground sub-

stance is insignificant in amount, and the connective tissue cells are scanty and are confined to the white fibrous sheaths in which the elastic fibres are enveloped. The elastic fibres are of very large size (10 to 15 μ) as compared with those of other forms of connective tissue. But, except for their larger size, these fibres have the same peculiar characteristics as the elastic fibres of areolar tissue. In their straight course, frequent branches, and their

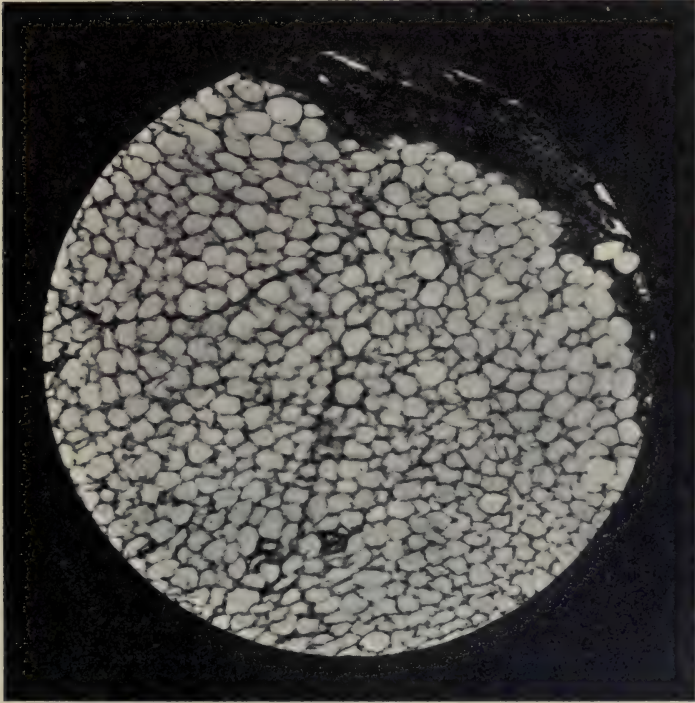


FIG. 43.—ADIPOSE TISSUE OF MAN.

The fat has been removed and only the cell membranes and investing connective tissue remain. Hematein and eosin. Photo. $\times 150$.

glistening, highly refractive appearance, as also in their characteristic reactions to specific dyes and other reagents, these fibres are identical with the elastic fibres of the other types of connective tissue.

The elastic fibres are bound together by delicate sheaths of very fine white fibres, and are united into bundles by coarser bands of fibrous tissue. Elastic tissue is found in the ligamentum sub-

flava, and in the ligamentum nuchæ of quadrupeds." In these locations it occurs in considerable quantity and has a peculiar yellowish color; it is for this reason that it is frequently described as *yellow elastic tissue*.

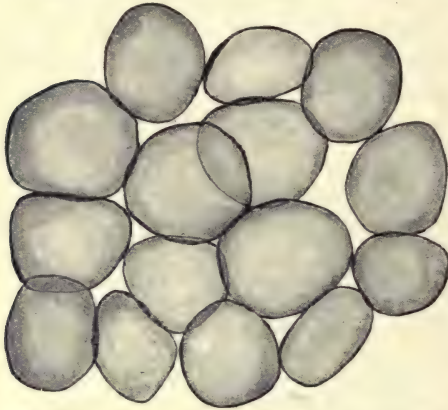


FIG. 44.—FAT CELLS FROM A TEASED PREPARATION OF ADIPOSE TISSUE OF MAN. $\times 110$.

Adipose Tissue (*fatty tissue, fat*).—Wherever areolar tissue occurs, adipose tissue may also be found; its distribution is therefore identical with that of areolar tissue. It forms a considerable mass, *panniculus adiposus*, beneath the skin of many parts; in it are embedded the kidneys, adrenals, and

many lymphatic nodes; the mesentery and omentum are freely supplied with fat. The same tissue is found in the grooves of the heart wall, and it also occupies the spaces of the mediastinum.

Adipose tissue is composed of *lobules* or groups of fat cells which are supported by fibrous bands and septa and are abundantly supplied with small blood-vessels.

The fat cells arise from the connective tissue cells by a deposit of fat droplets within the cytoplasm of the latter. These droplets continue to increase in number and fuse



FIG. 45.—ADIPOSE TISSUE.

The fat cells have been blackened by osmium tetroxid.
 $\times 110$.

with each other to form globules of increasing size, until the cytoplasm finally becomes so excavated as to form a mere limiting

membrane or cell wall. The nucleus is pushed to one side in this process and is flattened against the cell membrane; it is usually embedded in a remnant of granular cytoplasm. Being thus distended with fluid fat, the cell acquires a spheroidal shape.

During periods of starvation or malnutrition, at which time fat decreases greatly in volume, many of the fat cells return to a condition which approximates their former state. As the fat is removed the cytoplasm of the cell increases in amount, but assumes a peculiar fluid appearance and is not readily colored by the usual dyes. These cells, which still contain a number of fat droplets, are known as "serous" fat cells.

The origin of the fat cell is still somewhat in doubt. It was formerly thought that it might result from a deposit of fat within any of the connective tissue cells. A second theory considers that it arises only from a special fat-forming connective tissue cell. The demonstration of large numbers of peculiar ovoid granular cells within areas where fat cells were undoubtedly forming in fetal and young subjects, and the demonstration of similar cells in areas showing fat formation in adult tissues, has lent support to the hypothesis that these granular cells are the only progenitors of the fat cells (Shaw*).

Reticular Tissue (*reticulated tissue, reticulum*).—Reticular tissue occurs as the stroma of adenoid tissue in the lymphatic glands and other lymphoid organs, and, according to Mall,† is also found in the membrana propria of the secreting tubules of the stomach, intestine, kidney, testis, and thyroid, and in the marrow of bone and walls of the pulmonary air sacs.

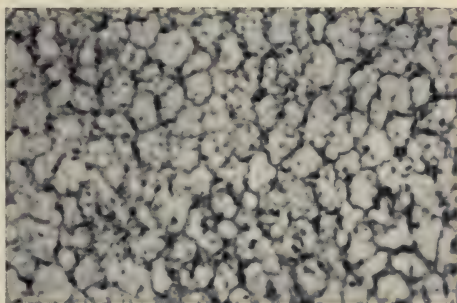


FIG. 46.—DEVELOPING ADIPOSE TISSUE FROM THE SUBCUTANEOUS TISSUE OF AN INFANT.

The fat has been removed by immersion in alcohol and ether. The polygonal outlines of the fat cells are well shown. Within many of them is seen the finer cytoplasmic network by which the inclosed droplets of fat were invested; this network had not been completely replaced by the accumulation of fat. Hematein and eosin. Photo. $\times 325$.

* J. Anat. and Physiol., 1901.

† Johns Hop. Hosp. Rep., 1896.

Like the other connective tissues, reticular tissue consists of cells, fibres, and ground substance; the latter, however, is no more

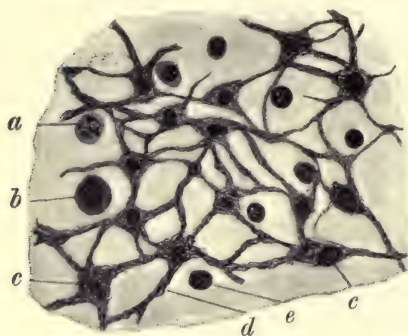


FIG. 47.—RETICULUM OF A CERVICAL LYMPHATIC NODE OF MAN, FROM A THIN SECTION FROM WHICH THE LYMPHATIC CORPUSCLES HAD BEEN PARTIALLY WASHED OUT.

a, polynuclear lymphatic corpusele; *b*, large mononuclear cell; *c*, connective tissue cells of the reticular tissue; *d*, fibrous bundle of the reticulum; *e*, small mononuclear lymphatic cell. Hematein and eosin. $\times 500$.

than a fluid tissue juice which, at least in the lymphoid organs, is identical with the lymph. The fibres are extremely fine and are arranged in slender bundles, which freely anastomose to form a delicate close-meshed reticulum. Individual fibres can be readily demonstrated in these bundles only after the action of alkalis, digestion by artificial gastric juice, or by other methods of dissociation, yet on careful examination indications of fibrillar structure can be seen in the reticulum of fresh tissue and in ordinary microscopical preparations. The chemical reactions of the reticular fibres are similar to

those of white fibres except that the former are much less readily digested by artificial gastric juice.

Flattened connective tissue cells clasp the bundles of reticular fibers; they are mostly found at the intersections of the anastomosing bundles. This fact was accountable for the former theory, which regarded reticular tissue as formed by the anastomosing branches of stellate cells. The careful investigations of Carlier* and others have shown the true nature of the lamellar cells and their underlying fibre bundles.

The fibres of reticular tissue very closely resemble the white fibres of areolar tissue, but differ from them in having a clearer, more highly refractive appearance. Their digestion in pepsin begins only after an interval of two hours, while white fibres are digested in a few minutes; they also stain less readily than white fibres, and yield reticulin, which differs somewhat from the gelatin of fibrous tissue. The intimate histologic relation between reticular and white fibrous tissue is shown by the fact that the two tissues are frequently continuous.

* J. Anat. and Physiol., 1895.

Mall * has recently attempted to show that reticular tissue should be considered as that form of connective tissue which has been least differentiated from the embryonic mesenchymal type. He accordingly considers the cells of the reticulum as formed by the

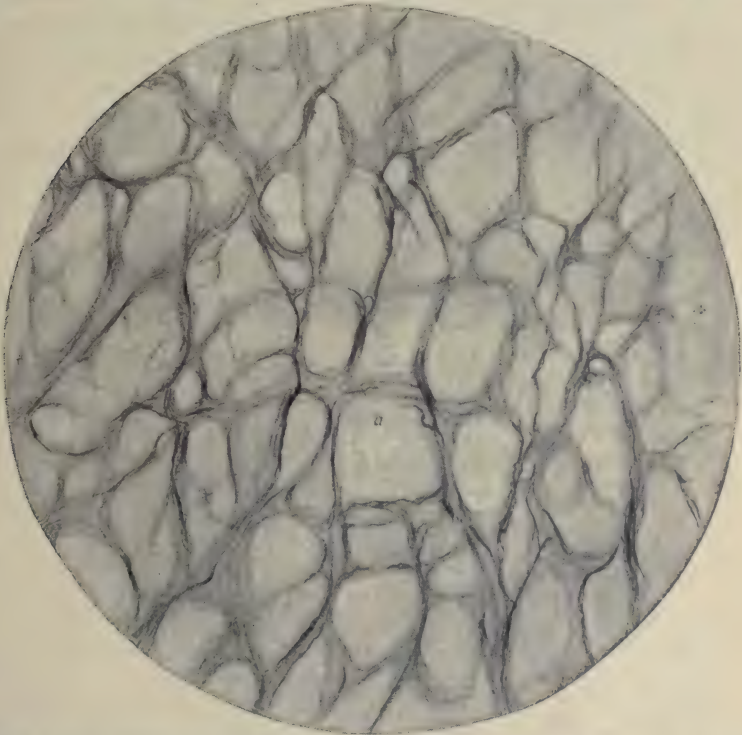


FIG. 48.—RETICULUM FROM THE MUCOSA OF THE FUNDUS REGION OF THE DOG'S STOMACH.

The section was made parallel to the surface and the glandular tissue removed by shaking in water. Picro-carmin. $\times 125$. (After Mall.)

undifferentiated endoplasm, and the reticular fibres as representing the specialized exoplasm of this most primitive type of connective tissue.

Lymphoid Tissue (*adenoid tissue*).—Lymphoid tissue is a reticular tissue the meshes of whose network are occupied by a closely packed mass of small spheroidal cells, the lymphatic corpuscles. These cells have a prominent ovoid nucleus which is richly supplied with chromatin and is occasionally indented, constricted, or

* Am. J. of Anat., 1902.

even polymorphous. In the latter case it consists of two or more lobules united by a chromatin filament. The amount of cytoplasm which surrounds the nucleus is variable, but never very great.

The lymphatic corpuscles* are so closely packed that it is almost impossible to distinguish the fine lines of the reticular stroma, except in those portions where some of the lymphatic cells have been washed out or displaced in the preparation of the specimen. The density of the lymphoid tissue varies much, however, in different organs and even in different portions of the same organ. The denser accumulations of lymphoid corpuscles may form either ovoid *lymphatic nodules* or *follicles*, or long dense trabeculae, the *lymphatic cords*, which are surrounded by looser portions of lymphoid tissue.

Lymphatic corpuscles are frequently infiltrated into the connective tissue of the mucous membranes, where they form irregular

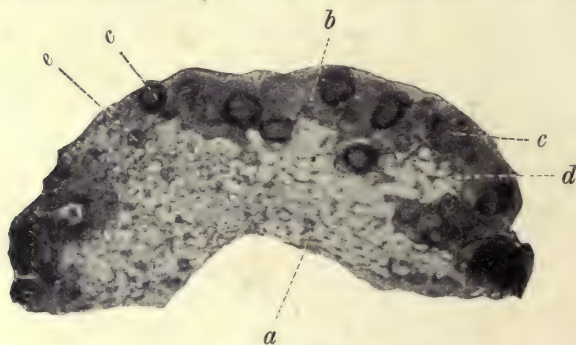


FIG. 49.—A LYMPHATIC NODE OF A DOG, SHOWING LYMPHATIC NODULES AND CORDS.

The lymphatic corpuscles have been partially removed from the medulla. *a*, medulla; *b*, cortex; *c*, nodules in the cortex; *d*, cords in the medulla; *e*, a fibrous trabecula. Hematein and eosin. Photo. $\times 20$.

collections, which may be termed *diffuse lymphoid tissue*, in contradistinction to *compact lymphoid tissue*, which occurs in the lymphatic glands, tonsils, thymus, and spleen, and in Peyer's patches and the solitary follicles of the intestinal tract. Diffuse lymphoid tissue is found in the mucous membranes of (*A*) the respiratory tract—nose, naso-pharynx, larynx, trachea, and bronchi; and (*B*) the alimentary tract—mouth, tongue, pharynx, esophagus, stomach, and intestines.

* For the several types of lymphatic corpuscles see Chapter X.

Blood and Nerve Supply of the Connective Tissues.—The connective tissues, but especially the areolar variety, form a supporting substance through which the various blood and lymphatic vessels and nerve trunks are distributed to all portions of the body. Within the connective tissues these vessels are everywhere present, and from them the connective tissue itself receives its supply of capillary vessels and terminal nerve fibrils.

The vascular supply of the connective tissues is very abundant. Small arteries, which are derived from the main trunks, form a capillary plexus throughout the tissue, the capillaries finally reuniting to form the venules.

It is in this capillary plexus that the fluid portions of the blood exude into the surrounding perivascular lymphatic or tissue spaces of the connective tissue. The tissue juices which arise in this manner are most active agents in the physiological processes of assimilation. From the tissue juice spaces, lymph re-enters the abundant capillary lymphatic vessels to be finally returned to the venous blood. Of the several varieties of connective tissue, the adipose possesses the most abundant blood supply; the lymphoid, on the other hand, is most richly supplied with lymph.

Abundant nerves are distributed to the connective tissues, some of which supply its blood vessels while others terminate in special forms of sensory nerve end organs.

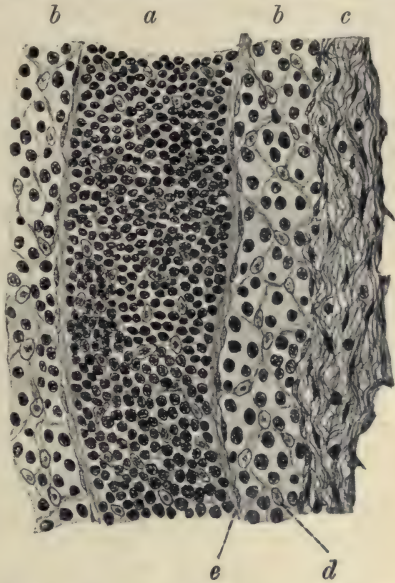


FIG. 50.—FROM A SECTION THROUGH THE MEDULLA OF A CERVICAL LYMPHATIC NODE OF MAN.

a, a "cord" of dense lymphoid tissue; *b*, looser lymphoid tissue of the medullary sinuses; *c*, the margin of a fibrous trabecula; *d*, nucleus of the connective tissue reticulum; *e*, endothelial lining of the lymphatic sinus. Hematein and eosin. $\times 475$.

CHAPTER IV

CARTILAGE

CARTILAGE is a dense, firm, but elastic substance, resembling connective tissue in that it is developed from similar mesoblastic cells. It contains a ground substance, the cartilage matrix, and at times fibres, which may be either white fibres or yellow elastic. The presence, absence, or character of these fibres determines the variety of cartilage. Three varieties are thus distinguished: *hyaline cartilage*, in which no fibres can be demonstrated within the matrix; *elastic cartilage*, whose matrix is permeated by yellow elastic fibres; and *fibrocartilage*, whose matrix contains white fibers.

HYALINE CARTILAGE.—This is the most abundant of the three varieties. It is found in the respiratory system, forming the cartilages of the nose, larynx, trachea, and bronchial tubes; in the costal cartilages of the ribs; as articular cartilages covering the ends of long bones; and in embryo, where, in the course of development of the bones, the entire skeleton, excepting only the flat bones of the skull and face, at first consists of hyaline cartilage. In most of these locations the cartilage occurs as plate-like masses, which are surrounded or encapsulated by a vascular membrane of dense fibrous and elastic tissue. This membrane is the *perichondrium*. The inner portion of this membrane is richly supplied with small cells, and it is from this cell layer that the cartilage is presumably developed. These chondrogenetic cells multiply, and deposit about themselves the structureless mass which first forms merely a capsule to the cell, but which, as it increases in amount, separates the various cells by wider areas and becomes the cartilage *matrix*. The cells, which in the perichondrium are small and decidedly flattened, likewise increase in size during this process, and become more nearly spherical, so that those *cartilage cells* which lie near the center of the cartilaginous plates are spheroidal in shape, while those toward the surface are

more and more flattened or elongated, their long axes gradually revolving from a perpendicular in the center of the plate until at the surface it becomes parallel with the perichondrium. Each cartilage cell is inclosed within a small space or lacuna, which during life it entirely fills.

Cell multiplication within the cartilage is peculiar in that cell division occurs within a firm capsule and results in the forma-



FIG. 51.—TRANSECTION OF A PLATE OF HYALINE CARTILAGE, FROM THE TRACHEA OF A CHILD.

The margin of the fibrous perichondrium can be seen on either side of the plate of cartilage, in the upper right hand corner and lower left hand corner of the figure. Hematein and eosin. Photo. $\times 400$.

tion of two daughter cells, which at first lie within the same encapsuled space. These two cells may each again undergo division within the same space with formation of four new cells. As a result of this peculiar method of cell division the cartilage cells are arranged in groups of two, four, or even eight cells. Each of the cells in the group deposits its capsule, and thus forms a

matrix about itself, so that the increasing space thus produced between the cells of a group may separate them until they become completely isolated cartilage cells each within its own *lacuna*. In this way the matrix of the cartilage is produced. The matrix of hyaline cartilage is devoid of fibrous or cellular structure.

During life, or if the tissue is examined in the fresh state, the cartilage cell entirely fills the lacuna in which it lies. But shortly after death shrinkage of these cells begins, so that after some

hours a considerable space intervenes between the cell and the wall of its lacuna. It has been supposed that this space was occupied during life by lymph. It would, however, seem more probable that it is partially the result of post-mortem shrinkage of the cell.

Frequently, and especially in developing cartilage, concentric lines may be seen surrounding each lacuna. These lines have been described as the "*cell capsule*." They appear only to indicate the successive layers of material which have been deposited by the

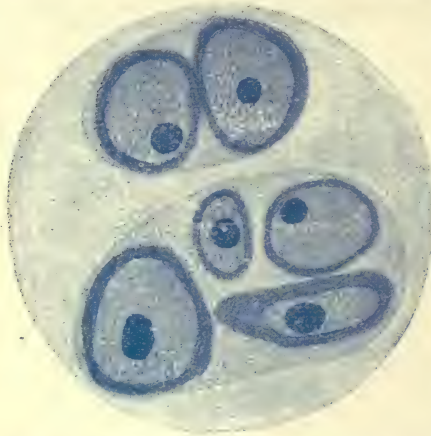


FIG. 52.—CELLS AND MATRIX OF HYALINE CARTILAGE FROM THE WALL OF A LARGE BRONCHUS OF MAN.

The grouping in pairs and fours, and the tendency to produce a so-called "capsule," are especially noticeable. Hematein. $\times 550$.

cell, and which have fused together to form its surrounding matrix.

Recent investigations on the development of the connective tissues suggest that cartilage arises from a mesenchymal syncytium in which the matrix is formed from the exoplasm of the syncytial tissue, the cartilage cell representing its endoplasm. The so-called capsule of the cartilage cell would accordingly represent the partially modified border line between the original endo- and exoplasm, and would thus correspond to similar conditions which are observed in other forms of developing connective tissue.

Cartilage cells frequently contain small droplets of fat, and these may coalesce until the cell is completely transformed into a fat cell. Isolated masses of adipose tissue, resulting from the

transformed groups of cartilage cells, thus make their appearance within the cartilaginous plates. This fatty metamorphosis is most marked in the elastic variety of cartilage.

By coloration with iodine, glycogen granules may also be demonstrated in the cartilage-cells (Ranvier *).

THE PERICHONDRIUM is a dense fibrous membrane which surrounds each individual plate-like mass of cartilage. It is continuous with the surrounding connective tissue, and is well supplied with blood vessels and lymphatics; it may also contain terminal nerve fibrils.

The cartilage itself is an absolutely bloodless and nerveless tissue. Neither are lymphatic channels demonstrable within the cartilage matrix. After long maceration or artificial digestion the matrix assumes a granular or fibrous appearance, and small channels have been demonstrated within it, which have been said to connect the various lacunæ; but it is evident that these appearances were possibly the result of artificial destructive processes, and could not therefore be considered as evidences of the presence of such structure in living cartilage.

ELASTIC CARTILAGE (*net cartilage, reticular cartilage*).—Elastic cartilage occurs within the human body in the external ear, and in the epiglottis and cartilages of Wrisberg and Santorini in the larynx. It resembles hyaline cartilage in the presence of large spheroidal cartilage cells and a homogeneous

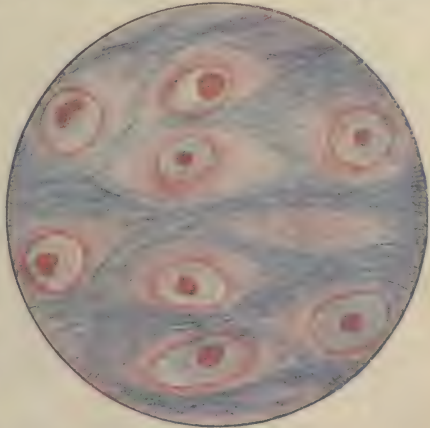


FIG. 53.—ELASTIC CARTILAGE FROM THE HUMAN EPIGLOTTIS, SHOWING THE LARGE OVOID CARTILAGE CELLS AND THE VERY DELICATE RETICULUM OF ELASTIC FIBRES.

Ehrlich's triacid stain. $\times 550$.

matrix, but the matrix is everywhere permeated by a dense interlacing network of fine *elastic fibres*. These plates of cartilage, like those of the hyaline variety, are surrounded by a dense fibrous perichondrium. Neither blood vessels, nerves, nor lymphatics are distributed within the matrix of elastic cartilage.

* *Traité technique d'histologie*, 2 éd., page 235.

FIBROCARILAGE.—This tissue forms the interarticular cartilages of the lower jaw, the clavicle, and the knee; composes the intervertebral disks and the other cartilaginous symphyses of the body; lines the tendon grooves of the bones, and forms the glenoid ligament of the shoulder and the cotyloid ligament of the hip. Fibrocartilage is intermediate in structure between hyaline cartilage and such very dense white fibrous tissue as occurs in the tendons of muscles. At the attached margin of the cartilaginous plates its tissue is continued by imperceptible

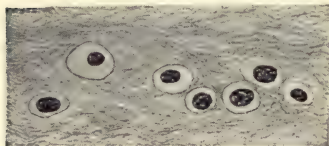


FIG. 54.— WHITE FIBROCARILAGE, SHOWING A GROUP OF OVAL CARTILAGE CELLS.

From the semilunar cartilage of the knee of man. Hematein and eosin. $\times 550$.

tissue is continued by imperceptible gradations into the surrounding fibrous connective tissues. Like the other forms of cartilage, this variety is also non-vascular and devoid of nerves.

Microscopically, fibrocartilage differs from such dense white fibrous tissue as is found in the ligaments and tendons, in that the meshes of the dense fibrous tissue of fibrocartilage are everywhere permeated by a hyaline matrix, in which, here and there, are small groups of ovoid cartilage cells. Each cartilage cell is occasionally surrounded by a characteristic, concentric, lamellar appearance of the adjacent matrix, the so-called "capsule."

Plates of fibrocartilage, unlike the other varieties, are not surrounded by a perichondrium.

CHAPTER V

THE MUSCULAR TISSUES

THE musculature of the body includes not only the skeletal muscles, but certain portions of the wall of the hollow viscera, such as the respiratory, alimentary, and urinary tracts. The skeletal muscles contain the most highly developed type of muscle cell, the visceral organs the lowest or least differentiated type; the muscle of the heart is intermediate between these, and stands in a class by itself.

Thus we distinguish three types of muscular tissue, the voluntary or striated, the involuntary smooth or plain, and the cardiac. These types are all of mesoblastic origin, the first muscular tissue to make its appearance being the "myotomes" from which the striated fibres of the skeletal muscles are developed. Cardiac muscular tissue next appears, the anlagen of the visceral musculature being formed at a still later period. The completed development of the three types of muscle may be said to correspond, in a way, to the priority of their appearance, the smooth muscle cells being the least and the striated cells the most altered or differentiated from the primitive cell type.

The physiological classification of muscle into the voluntary and involuntary varieties, while it corresponds quite closely with the striated and smooth types of muscle cell, is not exactly coincident with this histological division. Inasmuch as the terms voluntary and involuntary refer not to any structural peculiarity of the cell, but rather to the form and mechanism of its nervous control, it is not to be expected that such a classification based upon its physiological relation to the nervous system would be identical with the histological types of muscle cell. Nevertheless, the striated type of muscle is found to be usually under voluntary, and the smooth and cardiac types under involuntary control.

SMOOTH MUSCLE TISSUE (*plain, non-striated, or involuntary*).—This type of muscular tissue consists of small fusiform

cells which are either directly united by cement substance or are held together by very delicate membranous lines of connective tissue. In the former case adjacent cells are frequently connected by very delicate protoplasmic fibrils, *intercellular bridges*.

Each **muscle cell** (*muscle fibre*) consists of a much elongated fusiform mass of finely granular cytoplasm which incloses a *rod-shaped nucleus*. The peculiar shape of this nucleus, together with its distinct nuclear wall and the distribution of its chromatin in coarse granules, separated by wide intervals of achromatic substance, is characteristic of this variety of muscular tissue. These



FIG. 55.—SMOOTH MUSCLE FIBRES FROM THE PIG'S STOMACH, ISOLATED IN EQUAL PARTS OF ALCOHOL, GLYCERIN, AND WATER. Unstained. $\times 410$.

peculiarities of the nucleus in connection with the affinity of the cytoplasm of the muscle fibres for certain acid dyes, e. g., eosin, serve to distinguish this variety of muscle from white fibrous connective tissue, with which it might otherwise be easily confounded.

The cytoplasm of smooth muscle cells presents fine longitudinal striations indicative of a subdivision into ultimate *fibrillæ*, a rearrangement of the cell protoplasm which is more characteristically developed in the higher types of muscle. Transverse striations are not seen. The nucleus is found in the center of the cell.

The surface of the cytoplasm is somewhat condensed, though a true cell membrane, comparable to the sarcolemma of the striated muscle cell, is wanting. The size of the smooth muscle cell is

variable. Its greatest diameter in the region of the centrally situated nucleus is from 5 to 10 μ , about the diameter of a red blood corpuscle. The length of the cell varies from 50 to 500 μ . As seen in transverse section these fibres vary in size from a mere

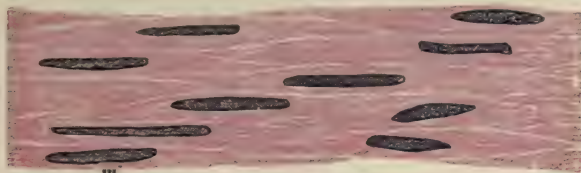


FIG. 56.—SMOOTH MUSCLE FIBRES FROM THE WALL OF THE HUMAN INTESTINE.
Longitudinal section. Hematein and eosin. $\times 665$.

point up to their maximum diameter, according as the section happens to pass through the end or through the middle of a fibre. Because of its central location, the nucleus is only found in the larger transections.

Smooth muscle fibers may be joined together in interlacing groups as in the wall of the uterus or bladder; or they may form broad membranous layers as in the wall of the alimentary tract; or again, they may form small isolated bundles, as in the skin. In any case, the muscle bundles are united by a delicate network of connective tissue.

Smooth muscular tissue occurs chiefly in the walls of the hollow or tubular viscera. Its **distribution** may be classified as follows:

(1) In the *alimentary tract*: lower portion of the esophagus, stomach, small and large intestines.

(2) In the *respiratory system*: trachea and bronchial tubes.

(3) In the *genito-urinary system*: ureter, bladder, urethra, penis, prostate, vagina, uterus, oviduct, and ovary.

(4) In the *vascular system*: arteries, veins, and the larger lymphatic vessels.

(5) In the *ducts of all secreting glands*: gall ducts and gall bladder, and the ducts of the pancreas, salivary glands, testicle, etc.

(6) It is also found in the capsules of the spleen and lymphatic nodes, in the skin, and in the intrinsic muscles of the eye.

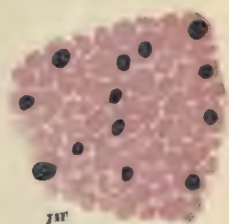


FIG. 57.—SMOOTH MUSCLE FIBRES FROM THE WALL OF THE HUMAN INTESTINE.

Transection. Hematein and eosin. $\times 750$.

CARDIAC MUSCLE.—The muscular tissue of the heart is intermediate in its phylogenetic position between smooth and striated muscle. Its cells consist of a granular cytoplasm which presents distinct longitudinal fibrillations, but only indistinct transverse striation. The latter appearance indicates an incomplete differentiation of its ultimate fibrillæ into alternate disks of light and dark (isotropic and anisotropic) substance, a differentiation which is much more highly developed in the striated variety of muscle.

The **cardiac muscle cell** is short and broad as compared with that of smooth muscle, and is joined to its neighbors at either end.



FIG. 58.—CARDIAC MUSCLE CELLS FROM THE PIG'S HEART, ISOLATED IN EQUAL PARTS OF ALCOHOL, GLYCERIN, AND WATER.

Unstained. (The nuclei are somewhat darker than they actually appear.) $\times 410$.

This firm union by abutment produces long bands, cardiac muscle *fibres*, which are united into bundles, and as such may be followed, by careful dissection, for long distances through the cardiac wall, their course maintaining a peculiar figure-of-eight direction. The union of cells end to end to form these fibres is accomplished by means of a cement substance, which is occasionally bridged across by fine protoplasmic fibrils. A cell membrane is wanting.

The cardiac muscle cell frequently branches, and its processes anastomose with those of adjacent cells to form a coarse network of muscle fibres, which insures harmony in physiological contrac-

tion. The numerous branches of its cells constitute the most prominent histologic characteristic of the heart muscle.

The **nucleus** of the cardiac muscle cell is oval in shape, and is situated in its center. Like that of smooth muscle, its nuclear

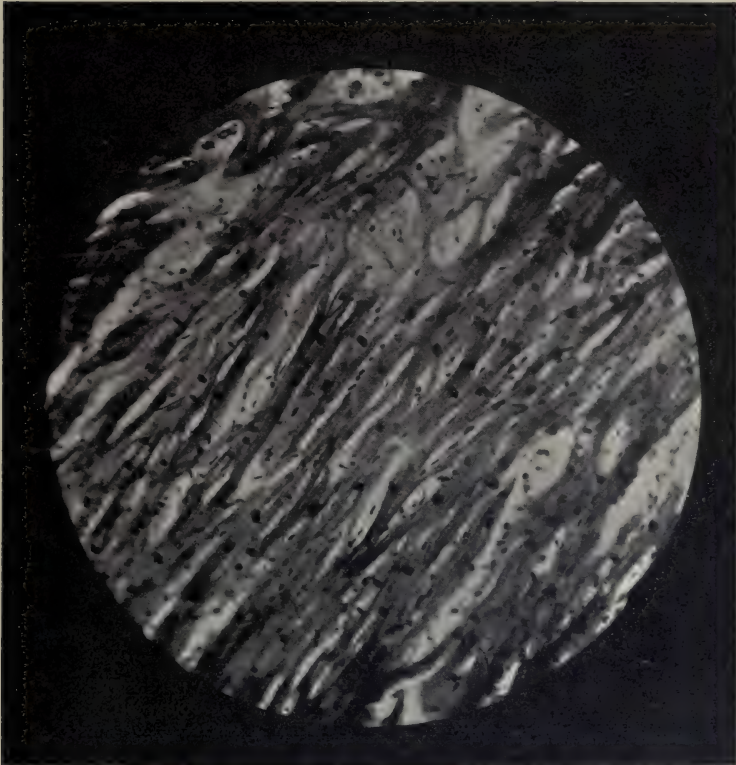


FIG. 59.—CARDIAC MUSCLE OF THE HUMAN HEART; THE ABUNDANT BRANCHES ARE PLAINLY SHOWN.

Longitudinal section. Hematein and eosin. Photo. $\times 120$.

wall is distinct and its chromatin is distributed in coarse, widely separated karyosomes.

The **cytoplasm** can be differentiated into a clear sarcoplasm and dim fibril bundles. The *sarcoplasm* is extremely translucent, which accounts for its apparently lighter color, and occurs most abundantly in the neighborhood of the nucleus. The *fibrils*, less translucent, and therefore darker in appearance than the sarcoplasm,

are prone to arrange themselves in rows, which, as seen in transection, appear to radiate more or less distinctly, from the central axis in which the nucleus lies, and toward the periphery of the cell.

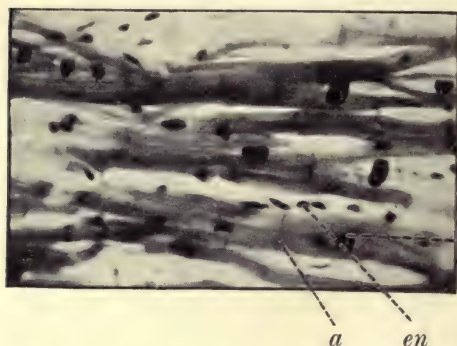


FIG. 60.—THE CENTRAL PORTION OF THE PRECEDING FIGURE, MORE HIGHLY MAGNIFIED.

a, cement substance uniting the ends of the muscle cells; this can also be seen at several other points and even in the preceding section if carefully studied; *en*, endothelium of the blood vessels; *Nuc*, nucleus of the cardiac muscle cell. Hematein and eosin. $\times 500$.

Heart muscle fibres occur in groups or bundles which are united by delicate membranes of connective tissue, the *endomysium*, whose finer fibres penetrate between the individual muscle cells. The normal amount of connective tissue occurring among the heart muscle fibres is, however, never very large. The bundles of muscle fibres, from the peculiar figure-

of-eight arrangement of the fibrous bands, characteristically interlace with one another, so that in sections from small pieces of the cardiac wall individual muscle fibres will be cut in all conceivable directions.

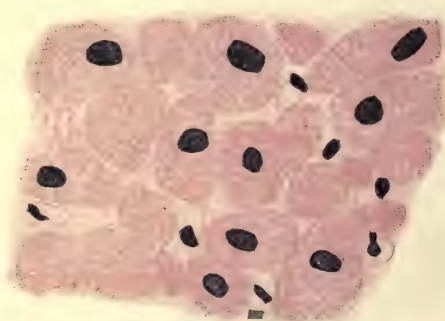


FIG. 61.—TRANSECTION OF A GROUP OF CARDIAC MUSCLE FIBRES FROM A PAPILLARY MUSCLE OF THE HUMAN HEART.

Hematein and eosin. $\times 550$.

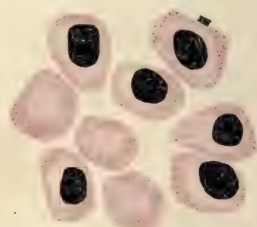


FIG. 62.—DEVELOPING MUSCLE FIBRES FROM THE HEART OF A HUMAN EMBRYO AT SEVEN MONTHS.

Fibrillæ are well developed at the periphery; the undifferentiated cytoplasm in the center presents a clear appearance and in some cases is partially occupied by the nucleus. Hematein and eosin. $\times 750$.

In certain heart muscle cells which are found just beneath the endocardium, and are more abundant in some of the lower mammals than in man (*Purkinje's muscle fibres*), the central mass of undifferentiated sarcoplasm is exceptionally abundant, the fibril bundles occurring only at the periphery of the cell. In many heart muscle cells a small number of very fine brownish *pigment granules* may be found in the sarcoplasm adjoining the nucleus.

STRIATED MUSCLE TISSUE (*voluntary muscle*).—The transversely striated cells of this form of muscle are the most highly differentiated of any of the three varieties. Their earliest anlagen are found in the myotomes of the body segments, in which the tissue consists of small elongated cells with a finely granular cytoplasm and a single centrally situated nucleus. These cells enlarge and soon present faint longitudinal striations. Coincident with these changes fibril bundles make their appearance at the periphery of the cell. At this stage the primitive muscle cell somewhat resembles the mature type of smooth muscle.

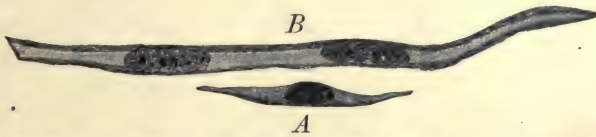


FIG. 63.—DEVELOPING MUSCLE FIBRES OF THE STRIATED VARIETY, FROM THE BUCCAL MUSCLES OF A FETAL PIG.

A, early stage, a "myoblast"; B, later stage, fibrillation has already begun at the periphery, but the central portion of the fibre is as yet undifferentiated; the fibre has been cut off at one end, the left. Hematein and congo-red. $\times 540$.

Further changes include the continued differentiation of the cytoplasm into fibril bundles, and the rapid multiplication of the cell nucleus without a corresponding division of the cytoplasm. During these changes, which are accompanied by differentiation of the primitive fibrils into light and dark disks, the muscle cells frequently resemble the mature cardiac muscle fibres with their indistinct striations. The progress and final consummation of these embryonic changes, with the consequent increase in the size of the cell, produce the mature striated muscle cell with its distinct membrane, its many nuclei, and its highly differentiated fibrillar cytoplasm.

The **striated muscle cell** is surrounded by a highly developed cell wall, the *sarcolemma*. This structure may be seen in transections of the muscle fibre, but is more clearly demonstrated in

teased preparations of fresh muscle fibres, in which the cell has been ruptured by gentle but firm pressure. The cytoplasm is frequently torn by this means, while the cell membrane, being of a more resistant nature, spans the interval between the ruptured ends of the cytoplasm.

Within the cell membrane the *cytoplasm* forms what may be termed a syncytium; the cell frequently attains an enormous size, being, as a rule, several centimeters in length but only 30 to 80 μ in breadth. Its shape is that of a long cylinder with rounded or very bluntly pointed ends.

The many *nuclei*, sometimes numbering hundreds for each muscle cell, are found at the surface of the fibre, lying just beneath the sarcolemma. The nuclei are ovoid in shape and possess a distinct nuclear wall and abundant chromatin. They are frequently surrounded by a narrow rim of undifferentiated cytoplasm, which is more abundant about the poles of the nucleus. The nuclei are also prone to accumulate at the ends of the fibre, at its insertion into the fibrous tissue of the tendon.

The cytoplasm of the striated cells is the most distinctly fibrillated of the several types of muscle fibre. The *ultimate fibrillæ* are arranged in small bundles, which are separated by intervals of clear undifferentiated *sarcoplasm*. As seen in cross section this arrangement of the fibril bundles gives rise to polygonal areas within the muscle cell, the dark ends of the cut fibrils being surrounded by lighter intervals of sarcoplasm. These peculiar polygonal outlines are described as the *areas* or *fields* of *Cohnheim*.

The distribution of the fibrils in bundles gives rise to distinct longitudinal striations, which are visible even with the aid of very

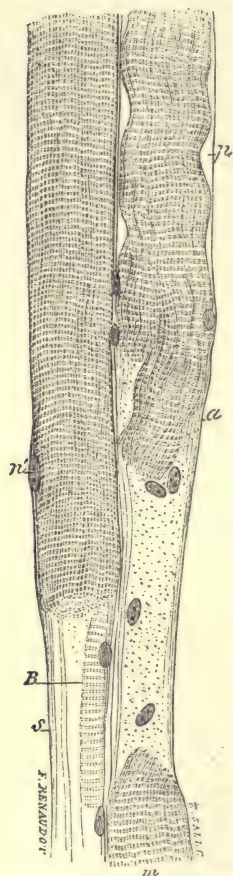


FIG. 64.—STRIATED MUSCLE FIBRES RUPTURED BY TEASING, SHOWING THE SARCOLEMA.

a, ruptured end of the muscle fibre; *B*, a bundle of fibrils projecting from the torn end; *m*, a muscle fibre; *n*, a nucleus of the muscle cell; at *p*, the muscle substance has shrunk away from the sarcolemma; *s*, sarcolemma. Moderately magnified. (After Ranvier.)

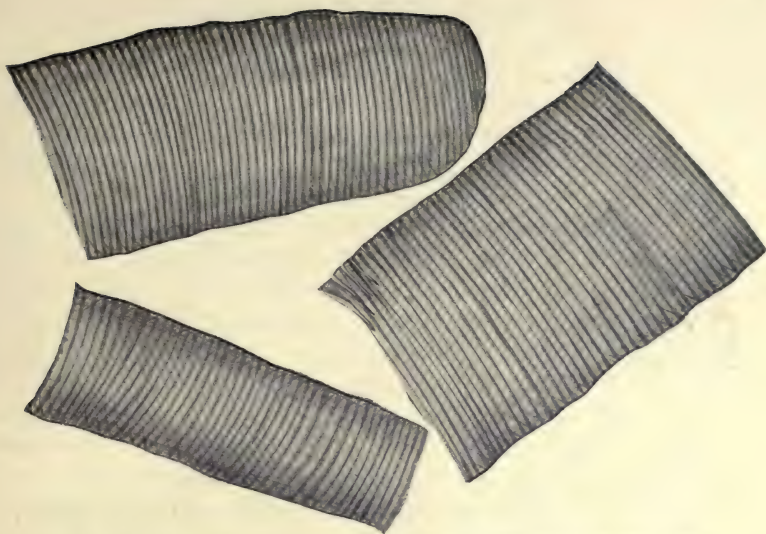


FIG. 65.—ISOLATED FRAGMENTS OF STRIATED MUSCLE FIBRES, UNSTAINED.
The one above is from the end of a fibre; that on the right shows at one end a tendency to cleavage into transverse disks. $\times 360$.

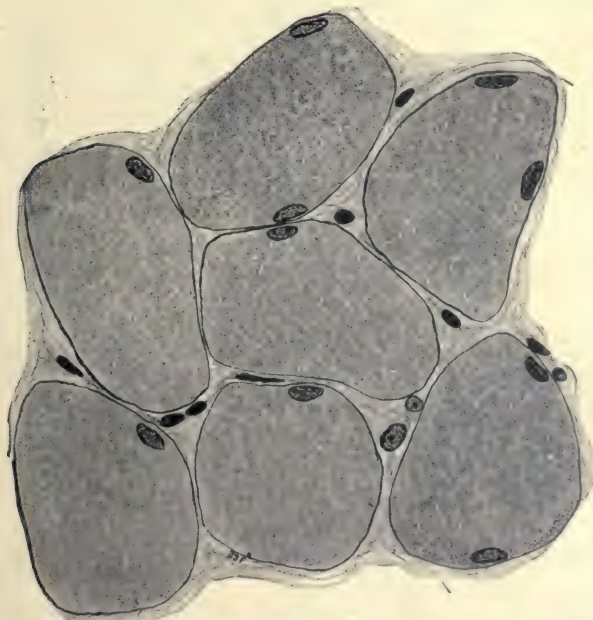


FIG. 66.—STRIATED MUSCLE FIBRES OF THE DOG, SEEN IN TRANSECTION.
The areas of Cohnheim are indistinctly outlined. Hematein and eosin. $\times 490$.

low magnification and even in living muscle fibres. When examined under higher magnification, after teasing, or in thin sections, the



FIG. 67.—A BIT OF A STRIATED MUSCLE FIBRE SEEN IN LONGITUDINAL SECTION.

The alternate light and dark cross striations are well shown. *h*, light line, Hensen's line, in the middle of the dark disk *Q*. *z*, dark line, Krause's membrane or Dobie's line, in the middle of the light disk. Hematein. $\times 1200$. (After Böhm and von Davidoff.)

readily visible under either low or high magnification as to become the most prominent characteristic of this type of muscle cell.

Regarding the **minute structure of the ultimate fibrillæ**, there is still much discussion. That the alternate light and dark disks are more than mere optical illusions is evidenced by the fact that they react differently to stains, notably to gold chlorid. Bisecting the middle of the dark disk, Hensen in 1868 described a fine light line, *Hensen's line*, and it is possible by the action of certain reagents, e. g., acids, alkalis, and artificial gastric juice, to produce transverse cleavage of the muscle cell along this line (Ranvier *).

fibril bundles can be seen to consist of numerous still finer fibrils, the *ultimate fibrillæ* (sarcous element of Bowman, sarcostyle of Schäfer). These ultimate fibrillæ are also seen to consist of alternate light and dark disks. When examined under polarized light the dark disks are found to be anisotropic or doubly refracting, the light disks isotropic or singly refracting.

The alternate light and dark disks are so disposed within the muscle cell that the corresponding disks of adjacent fibrillæ lie in the same transverse plane. This arrangement produces alternate light and dark composite disks whose diameter corresponds with that of the muscle cell. These larger alternate light and dark disks, each composed of the corresponding portions of innumerable ultimate fibrillæ, give rise to an appearance of *transverse striation* which is so



FIG. 68.—A SMALL PORTION OF A MUSCLE FIBRE OF A CRAB SHOWING BEGINNING SEPARATION INTO FIBRILS.

Drawn from a photograph. $\times 600$. (After Schäfer.)

* *Traité technique d'histologie*.

At about the same time Krause described a dark transverse line which bisected the light disk. This line, the membrane of Krause (Dobie's line), may be readily seen under ordinarily high magnification. The interpretation of this appearance, however, is somewhat doubtful. Following its description by Amici in 1859 and Krause in 1868, it was considered that a complete membrane bisected the light disk, but this conclusion was discredited by the observations of Dobie, Kühne, and others, and is strenuously opposed by Schäfer, who regards Krause's membrane as the optical expression of a row of dark dots or granules disposed in one transverse plane, each dot lying in the angle between adjacent areas of undifferentiated sarcoplasm.

Striated muscle cells *rarely branch*, yet in those locations where its fibres are inserted into the subcutaneous or submucous connective tissue, e. g., the face, scrotum, tongue, etc., branching fibres frequently occur.

Within the muscles the individual cells are united by a delicate connective tissue *endomysium* which penetrates between the fibres and supports a liberal supply of capillary vessels. The muscle fibres are, however, unequally distributed within the muscle, numbers of muscle cells being united to form fibre bundles or *fasciculi*, which are surrounded by thicker membranes of connective tissue, the *perimysium*. The fasciculi are in turn united by bands of connective tissue derived from a firm fibrous membrane, the *epimysium*, which surrounds the entire muscle.



FIG. 69.—FIBRILS FROM THE WING MUSCLES OF A WASP.

A, contracted; B, stretched; C, uncontracted. The alternate dark and light disks are prominent; the membrane of Krause in the light disk, and the line of Hensen in the dark disk are well shown. Very highly magnified. (After Schäfer.)

Blood and Nerve Supply.—The muscular tissues are richly supplied with nerves, blood vessels, and lymphatics. The larger

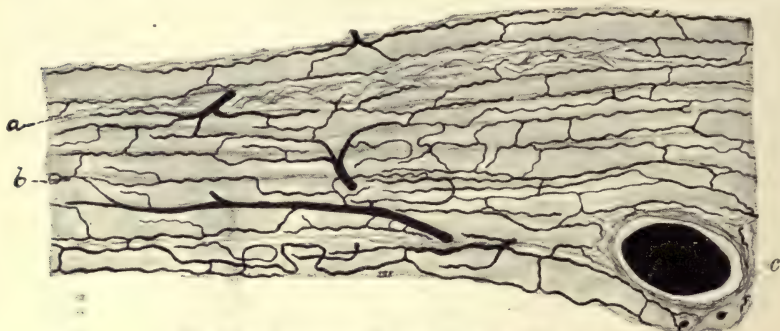


FIG. 70.—STRIATED MUSCLE FIBRES OF THE DOG.

The blood vessels have been filled by injection with a gelatinous mass and are represented in black. One whole fasciculus and one fibre from an adjacent fasciculus have been included. *a*, perimysium; *b*, endomysium; *c*, a large vein seen in transection. The section was not stained. $\times 80$.

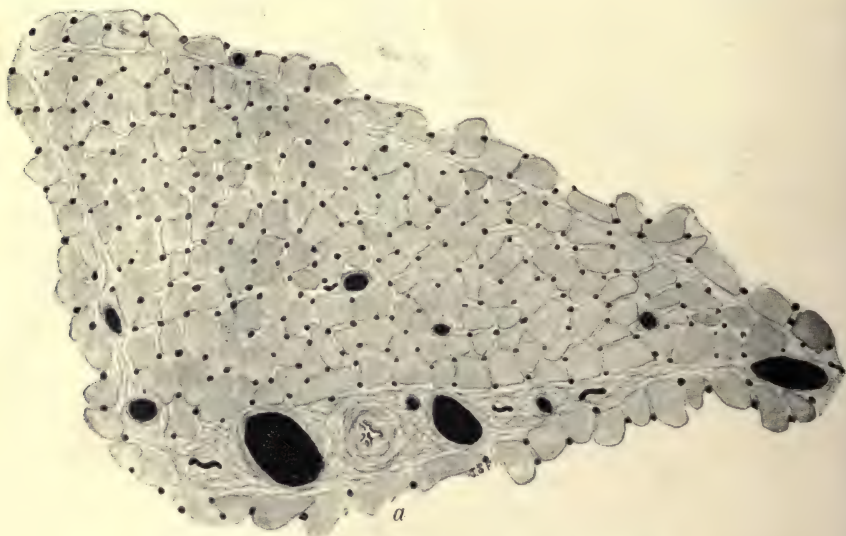


FIG. 71.—STRIATED MUSCLE OF A CAT SEEN IN TRANSECTION.

The blood vessels have been injected and are black in the figure. At *a* an artery is contracted and empty. The heavy black vessels are veins and arterioles; the small black dots are capillaries in transection. One whole fasciculus is represented and is surrounded by a delicate perimysium of connective tissue. Between the muscle fibres is the still more delicate endomysium. The larger vessels are almost exclusively found in the perimysium. The section was not stained. $\times 80$.

nerve trunks are found in the loose connective tissue which surrounds the muscle, and in the epimysium and perimysium. From these trunks fine branches enter between the muscle fibres and break up into a plexus of delicate fibrils. The terminations of the nerve fibres are found within the sarcolemma of the muscle cell as the *motor end plates* and, in striated muscle, as the terminal filaments of special sensory endings, the *muscle spindles*.*

The *blood vessels* also distribute their larger trunks within the connective tissue of the epimysium. The smaller branches penetrate the endomysium and supply a rich capillary plexus with long rectangular meshes. This network of capillaries surrounds the

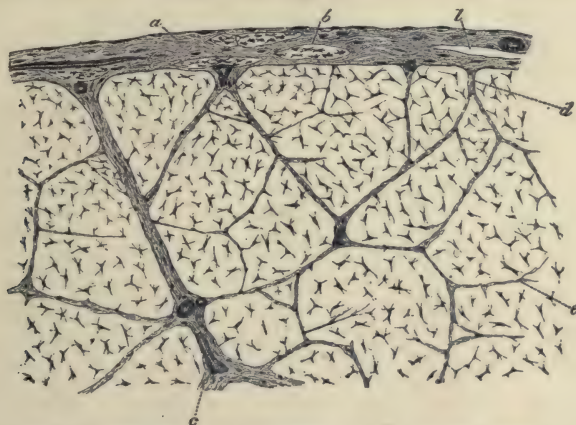


FIG. 72.—PORTION OF A TRANSECTION OF A LARGE TENDON.

a, fibrous capsule with circular, and at *b*, longitudinal bundles of connective tissue; *c*, *d*, and *e*, fibrous septa between the fasciculi of the tendon; *f*, lymphatic cleft. Moderately magnified. (After Schäfer.)

muscle cells so completely that each cell is placed in relation with four or five capillary vessels which run parallel with the long axis of the cell.

Numerous *lymphatics* occur in the perivascular connective tissue. These lymphatic vessels are especially abundant in the cardiac muscle.

The distribution of the blood and nerve supply of cardiac and smooth muscle closely resembles that of the striated variety. The larger trunks are found only in the thicker connective tissue membranes, but the smaller nerve trunks and capillary vessels

* See chapter on the Peripheral Nerve Terminations.

penetrate between the individual fibres of the cardiac muscle and between the smaller fibre bundles of smooth muscle.

The **TENDONS** of the striated muscles consist of parallel bands of dense white fibrous tissue, between whose bundles are found rows of flattened connective tissue cells, which are frequently much enlarged and have a peculiar oblong shape.

At the junction of the tendon with muscle each small bundle of tendon fibres becomes continuous with the sarcolemma of a muscle cell, the end of the tendon bundle being concave to receive the rounded end of the muscle fibre. At this end of the cell the muscle nuclei are especially abundant.

Table showing the more important differential characteristics of the several varieties of muscle cells.

	STRIATED.	SMOOTH.	HEART.
Longitudinal fibrillæ.	Marked.	Present.	Distinct.
Transverse striations.	Marked.	Absent.	Present.
Nucleus { Number	Numerous.	One.	One (or two).
{ Shape	Ovoid.	Rod-shaped.	Ovoid.
{ Situation ..	Peripheral.	Central.	Central.
Branches.	Rare.	Rare.	Numerous.
Size { Length	Several cm.	Short (and slender).	Short (and broad).
{ Breadth... ..	40 to 100 μ .	5 to 10 μ .	30 to 50 μ .
Shape.....	Long cylinders.	Fusiform.	Short prisms (united to form long fibres).
Sarcolemma.	Present.	Absent.	Absent.

CHAPTER VI

BLOOD

THE blood is a bright red, semi-opaque fluid, which circulates within a closed system of vessels, the circulatory system. The blood may be considered as a primary tissue, whose peculiar cell elements are the blood corpuscles, and whose intercellular substance is the fluid blood plasma. Its corpuscles, according to their color, are of two varieties: those which are colored, the red blood cells, and those which are colorless, the white blood cells. To these must now be added the blood platelets, minute protoplasmic masses of definite form which are constantly present, and are therefore true structural elements of the blood, but which can as yet scarcely be classed as tissue cells.

When blood is removed from the body it immediately assumes a viscid consistence, and in a short time will solidify into a jelly-like mass, the blood clot. This peculiar property is part of the phenomenon of coagulation—a phenomenon which results from a rearrangement of the chemical constituents of the blood with the formation of a new histological element, the fibrin. Coagulated blood consists of corpuscles, fibrin, and a fluid serum which differs from the plasma in its chemical composition, though the two fluids are very similar in their histological appearance.

RED BLOOD CORPUSCLES (*colored blood corpuscles, red blood cells, erythrocytes*).—The red blood cells are minute circular disks with biconcave surfaces and rounded or convex edges. The color of the corpuscle differs according as they are viewed by reflected or by transmitted light. By reflected light they have a bright red color, by transmitted light a faint greenish-yellow or amber shade. This color is entirely due to the presence of hemoglobin within the corpuscle; the so-called shadows which remain after the hemoglobin has been dissolved out of the cell are absolutely devoid of color, and possess very little affinity for stains. Since all the hemoglobin of the blood is contained within these red cells, the

familiar red color of the blood is due to reflection of light from the surface of its innumerable colored corpuscles. The suspension in the blood plasma of a multitude of transparent disks which act in part as biconcave—center of the corpuscle—and in part as biconvex circular lenses—corpuscular rim—accounts in great measure for the opacity of thick layers of blood.

The average diameter of a red blood cell is $7.5\ \mu$ ($\frac{1}{3200}$ inch); its thickness varies from 2 to $4\ \mu$. These cells vary but little in size. Seventy-five per cent of the red cells in human blood will measure $7.5\ \mu$, the remainder are either a little smaller or a little larger than the average, the normal extremes being about $6\ \mu$ and $8\ \mu$ respectively. Those of extreme size are called *megalocytes*, while the smallest are *microcytes*.

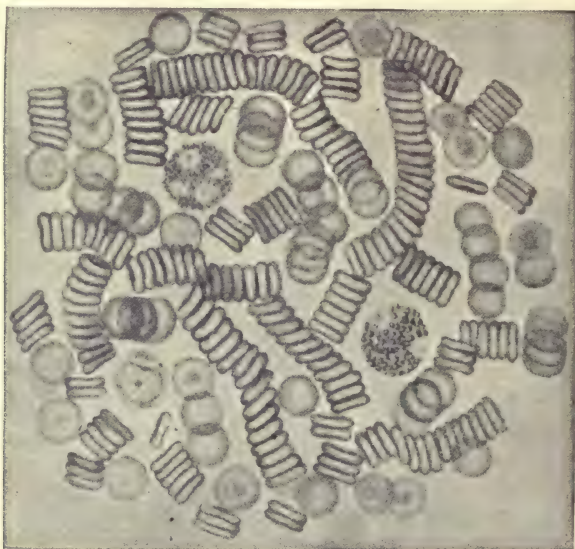


FIG. 73.—FROM A FRESHLY PREPARED, UNSTAINED SPECIMEN OF HUMAN BLOOD.

Three leucocytes, an eosinophile, a polynuclear, and a lymphocyte, are represented. Many red blood cells, some "on the flat," some in rouloux and in profile, are also shown. $\times 1200$, but reduced somewhat in reproduction. (After Schäfer.)

The number of red corpuscles in the blood is subject to constant variation between wide limits. Many physiological conditions influence their total number, as well as the relative proportion of red cells to the white. The average number of red blood cells in the adult male is about 5,000,000 per cubic millimeter. In

young robust persons the number may be considerably higher. The number may also be much reduced by considerable hemorrhages or by the imbibition of large quantities of fluid. Profuse perspiration tends to produce concentration of the blood and an apparent increase in the number of its corpuscles. The number of red blood cells in the female is slightly less than in the male, about 4,500,000 per cubic millimeter.

The red blood cell consists of a compound of hemoglobin with a colorless mass, the "*stroma*" of Rollett. The precise manner in which the hemoglobin is contained within this stroma has been the subject of considerable discussion. The recent investigations of G. N. Stewart* on the effect of laking reagents on the blood would tend to show that the hemoglobin is in part held in solution in the stroma, and in part in more intimate combination. That this stroma is not, as Rollett supposed, a structureless mass, may now be considered as satisfactorily demonstrated. Much evidence lately advanced tends to show that the red cell, though not possessed of a distinct cell membrane in the sense of Schwann, is nevertheless supplied with an *external limiting layer*, a thickened exoplasm, which is homogeneous in appearance, is insoluble in water, permits free osmotic currents, and probably contains the traces of lecithin and cholesterin which are found in the red blood cells.

Important information concerning the internal structure of the stroma is furnished by the fact that the large nucleated red blood cells of amphibians, as well as the early nucleated cells, erythroblasts, of man and mammals, have been shown to possess a reticular or alveolar structure. However, the living red blood cells of human blood under ordinary conditions show no trace of inter-

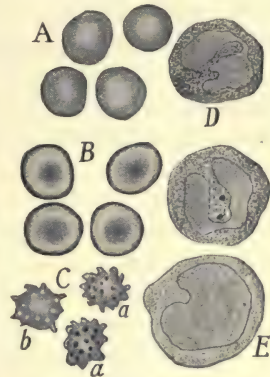


FIG. 74.—BLOOD CELLS FROM A SPECIMEN OF FRESHLY DRAWN UNSTAINED HUMAN BLOOD.

A, red blood cells, deep focus, showing a light center and dim margin; B, the same with a higher focus; the center, being slightly out of focus, is dim while the margin is light; C, crenated red cells from the margin of the preparation; a, deep focus; b, higher focus; D, two polynuclear leucocytes; E, large mononuclear leucocyte. $\times 750$.

*J. of Physiol., 1899; also J. of Med. Research, 1902.

nal structure, and in their mature form possess no semblance of a nucleus. Nucleated red blood cells in man are only found as premature forms in the hemopoietic tissues and in the circulating blood in early embryonic life. In the later periods of fetal life, and even in the first year of childhood, an occasional nucleated red cell may be demonstrated in the blood current. Diseased conditions, involving rapid regeneration of blood cells, are, however, frequently accompanied by the appearance within the general blood current of nucleated red cells, *erythroblasts*, in considerable numbers.

Effect of Reagents upon the Red Blood Cells.—The effect of certain reagents upon the red cells throws much light upon their finer structure, and especially upon their relation to osmotic processes. The red cells apparently exist within the blood, floating free in its plasma, in a state of osmotic stability; the plasma is then an *isotonic* solution as regards the red cell. Should the specific gravity of the blood plasma be in any way increased, it immediately becomes *hyperisotonic* for the red cell; should, on the other hand, the specific gravity be diminished, the plasma becomes *hypisotonic*. It should be borne in mind that osmotic flow occurs in a direction from the lighter toward the heavier fluid.

Water.—The addition of water to the blood plasma diminishes the specific gravity of the latter, and produces an osmotic flow into the red cells. The corpuscles promptly



FIG. 75.—SHOWING THE ACTION OF WATER UPON THE RED BLOOD CELL.

a, the cell in profile; *b-e*, various stages in the transformation which leaves only a "shadow" *e*; diagrammatic. (After Schäfer.)

swell, lose their biconcave shape, and finally, from the extreme distention, their limiting membranes apparently rupture and permit the escape of the hemoglobin; the remaining colorless stroma of the red cells forms the so-called "*blood-shadows*." The rapidity of these changes is apparently dependent upon the amount of water added to the

plasma, and therefore upon the degree of hypisotonicity produced in the latter.

Saline Solutions (hyperisotonic).—Solutions of sodium chlorid, magnesium sulfate, etc., whose specific gravity is greater than that of the blood plasma, when added to the blood produce a condition of hyperisotonicity. The consequent osmosis takes place from the corpuscle to the plasma; the corpuscular wall promptly collapses and presents an irregular spinous or serrated profile—

becomes *crenated*. The rapidity and extent of the collapse and consequent crenation appear to be dependent upon the degree of hyperisotonicity produced, and the consequent volume of the outward osmotic flow.

Normal Saline Solution (isotonic).—It is possible to produce a saline solution whose specific gravity corresponds with that of the plasma, and which is isotonic for the corpuscles. An aqueous solution of this character contains about 0.9 per cent of sodium chlorid. The exact strength of such a solution can not be accurately stated, for the reason that the tonicity of the blood plasma not only varies somewhat in different individuals, but also in the same individual at different times and under varying conditions of diet, absorption, excretion, etc.

An isotonic solution, when added to the blood, will be found to produce no visible change in the appearance of the blood cells.

Certain reagents, as well as extremes of heat and cold, have the property of rapidly dissolving out the hemoglobin, laking the blood, either by rupture or by solution of the corpuscular envelope. Such reagents are dilute acids or alkalis, bile, and the serum from a different species of animal; the last-mentioned reagent possesses a certain forensic value in determining the animal species of a given specimen of blood. These reagents, when mixed with human blood, produce a rapid destruction of its corpuscles—*hemolysis*.

These osmotic peculiarities, taken in connection with other facts—e. g., the presence of a cell membrane in the red blood cells of animals beneath the mammalian type; the extreme elasticity of the corpuscle, which can be distorted into almost any conceivable shape, but returns immediately to its original form; and the tendency of the corpuscles in undiluted blood to adhere to each other in the form of moniliform piles, rouleaux, like rolls of coin, their cohesion being apparently due to the presence in their envelope of cholesterin and lecithin, which possess the physical properties of a fat—would seem to demonstrate beyond a doubt the presence in the red blood cell of an outer exoplasmic envelope differing in structure and in composition from its contained endoplasm.

Development of the Red Blood Cell.—The earliest embryonic origin of the red blood corpuscle is a much disputed point. According to van der Stricht,* however, they first appear in the

* Compt. rend. soc. de biol., 1895.

"blood islands" of the extra-embryonic vascular area of the mesoblast. Their mode of origin in this location is essentially intracellular, through the medium of the "*vaso-formative cells*." This

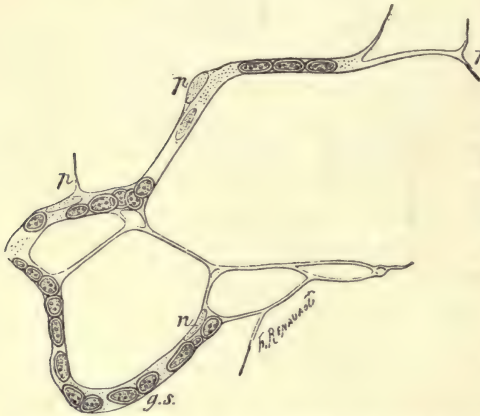


FIG. 76.—"VASO-FORMATIVE" CELLS FROM THE MSENTERY OF A RABBIT SEVEN DAYS OLD.

g.s., red blood cells; *n*, nucleus of the vascular endothelium; *p*, points of growth, at which extension occurs. Highly magnified. (After Ranvier.)

nucleated, hemoglobin containing cells within the primitive blood vessel.

Similar vaso-formative processes occur throughout the mesoblastic tissues in the early periods of fetal life. They have been carefully studied in the subcutaneous tissue and the omentum by Schäfer, Ranvier, Minot, Nicolaidès, *et als.*; but more recent observations by S. Mayer, E. Neumann, Spuler and Fuchs tend to throw discredit upon the previous conclusions, inasmuch as these



FIG. 77.—A "VASO-FORMATIVE CELL."

a, isolated red blood cell. Note the apparent disintegration of the red blood cells shown in the middle of the figure. (After Fuchs.)

observers maintain that the vaso-formative cells instead of being developing cells are in reality in a state of degeneration, they having been separated from the general vascular current by occlusion of the lumen. The small, hemoglobin containing, protoplasmic

process consists essentially in the enlargement and excavation of the vaso-formative cell groups, their nuclei undergoing division by mitosis, sometimes without corresponding division of the cytoplasm, the daughter nuclei forming in some cases primitive nucleated blood cells, and in others the nuclei of the endothelial wall. According to Ranvier, minute particles of the vaso-formative cytoplasm may separate from the parent mass to float free as non-

masses found within such cells and described by Ranvier as true microcytes are taken by these authors to be minute portions of the included red cells. Fuchs, especially, (see Fig. 77) describes the disintegration not only of the cytoplasm, but of the nuclei of occluded erythroblasts as well. The formation of red blood cells within the "vaso-formative" cells of the mesoblastic tissues, in the later periods of fetal life at least, must be considered as somewhat doubtful.

With the appearance of the fetal *liver*, at a very early period, the bulk of the hemopoietic function seems to be transferred to this organ, in the "blood-islands" of which, nucleated erythroblasts are rapidly formed by karyokinesis. The primitive *spleen* also assumes a small portion of the blood forming function. In neither of these organs, however, does this function appear to persist much beyond the term of intra-uterine life.

The appearance of the *red marrow of bone* marks the transfer of a steadily increasing portion of the hemogenic function to this tissue. Moreover, bone marrow seems to be the sole tissue in which the function persists throughout adult life. In this tissue the red blood cells are developed by mitosis, occurring within hemoglobin containing *erythroblasts*. This process is, however, confined to the marrow tissue proper, the red cells, after the disappearance of their nucleus, only secondarily gaining admission to the vascular channels* (Swaen et Brachet †). The disappearance of the nucleus of the daughter erythroblasts may possibly be the result of *extrusion* (Rindfleisch ‡), or more probably of solution (Köl liker §). In the latter case the nucleus is said to disappear by *karyolysis*; if during this process the chromatin becomes collected into a small compact mass, the nucleus is said to disappear by *pyknosis*.

The more important histological deductions from the foregoing facts may be stated as follows:

1. All red blood cells are in their primitive condition nucleated, viz., erythroblasts, and consequently biconvex rather than biconcave.

* In this connection the observation of Ascoli (Giorn. d. R. Accad. di Med. di Torino, 1899), that nucleated red blood cells are constantly present in the efferent tibial vein of the dog, is of interest.

† Arch. de biol., 1902.

‡ Arch. f. mik. Anat., 1879.

§ Handbuch der Anat.

2. In fetal life—and in certain diseased conditions—blood formation occurs with sufficient rapidity to permit the immature erythroblasts to gain entrance into the general circulation. The red blood cells of the earliest fetal circulation are therefore all nucleated, those of later fetal life are nucleated in constantly decreasing proportion, while in healthy extra-uterine life only mature non-nucleated forms occur in the general blood current.

3. The primitive nucleated red cells, the type having been once firmly established in the early fetus, are reproduced by mitotic division of similar parent cells.

4. Though the size of the primitive cells varies considerably, and is for the most part larger than that of the mature forms, yet prior to their entrance into the general circulation of the adult, all erythrocytes closely approximate a constant diameter of 7.5μ .

WHITE BLOOD CORPUSCLES (*white blood cells, leucocytes, colorless corpuscles*).—The white blood cells are nucleated granular masses of protoplasm usually of spherical form but possessing a remarkable tendency to undergo active amœboid motion. They are of a distinctly viscid consistence, adhering more or less closely to the vascular walls, and therefore lying at the periphery of the blood stream, while in circulation. In microscopical preparations of freshly drawn blood they adhere quite firmly to the glass slide or cover. With moderately high magnification the cytoplasm of the white blood cell is seen to possess fine granules which vary in number and in size in different cells. The greater portion of these cells possess numerous fine granules (neutrophiles); a smaller portion show no cytoplasmic granules in freshly prepared specimens (the non-granular, “hyaline” or mononuclear leucocytes); occasional cells show very coarse granules throughout their cytoplasm (eosinophiles).

All forms of white blood cells possess a nucleus which, however, is only faintly visible in the living cell, but is readily brought into view by the action of dilute acids, which also cause the cytoplasmic granules to accumulate about the nucleus. The nucleus is likewise brought into view by other laking reagents—water, bile, electricity, etc., as well as by hyperisotonic solutions—heavy solutions of sodium chlorid, etc.

Normal blood contains 6,000 to 8,000 white blood corpuscles per cubic millimeter. They are therefore present in the proportion of 1 to 600 or 800 red corpuscles. This ratio is, however,



FIG. 78.

FIVE NUCLEATED RED CELLS FROM THE BLOOD OF A FROG.

Eosin-methylen blue. Hasting's method. $\times 1200$.

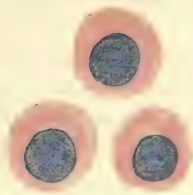


FIG. 79.

THREE NUCLEATED RED BLOOD CELLS FROM THE MARROW OF A HUMAN RIB.

Eosin-methylen blue. Nocht method. $\times 1200$.

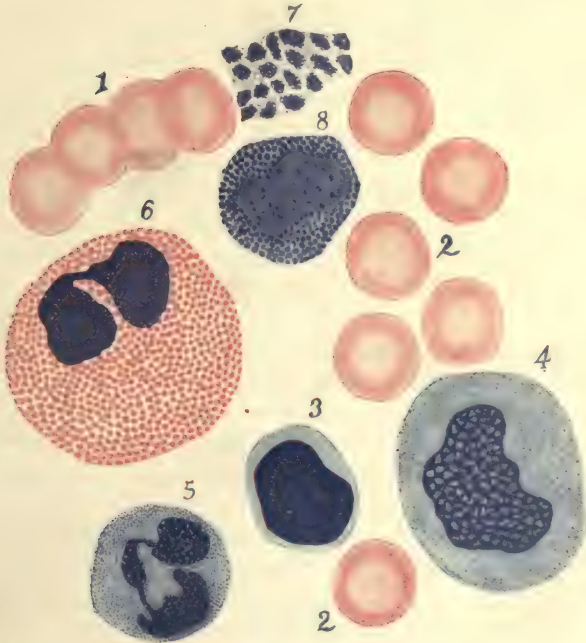


FIG. 80.

A GROUP OF CELLS FROM NORMAL HUMAN BLOOD.

1, red blood corpuscles in rouleau formation; 2, red blood corpuscles, surface view; 3, lymphocyte; 4, large mononuclear leucocyte; 5, polynuclear, finely granular leucocyte; 6, eosinophile leucocyte; 7, a group of blood platelets; 8, basophile leucocyte. Eosin-methylen blue. Hasting's method. $\times 1200$.

subject to constant variations from physiological causes, e. g., digestion, absorption, etc.

Varieties of White Blood Corpuscles.—After fixation and staining the nucleus, as well as the cytoplasmic granules, is found to present characteristic differences in the several varieties of white blood corpuscle. The nuclei of the non-granular cells—mononuclear leucocytes—are spheroidal in shape, have a fairly distinct nuclear membrane, and possess a varying amount of irregularly distributed chromatin. The size of the nuclei of these cells is also variable, and upon these differences two cell types are recognized, the large and the small mononuclear.

The *small mononuclear leucocytes*—lymphocytes—possess a highly chromatic and therefore deeply staining nucleus of small size which occupies nearly the entire cell, the encircling rim of cytoplasm being extremely narrow and at times scarcely demonstrable. The *large mononuclear cells*—“spleenocytes” of Virchow—possess a wider cytoplasmic rim and a large nucleus with a distinct nuclear wall; the nucleus in contradistinction to that of the lymphocyte is deficient in chromatin, and therefore is but lightly stained with nuclear (basic) dyes.

The cytoplasm of the mononuclear cells under moderate magnification presents a hyaline structureless appearance, but with higher magnifying power a delicate reticulum and at times, especially in the large mononuclear forms, very fine neutrophile granules can be demonstrated.

The nucleus of the mononuclear forms, but much more frequently that of the larger variety only, occasionally deviates from its typical spheroidal form, being notched, indented, or even of almost a horseshoe shape. In this latter form these nuclei somewhat resemble those of the polynuclear cells to be described, yet they are readily distinguished therefrom by their characteristic deficiency in nuclear chromatin and cytoplasmic granules.

The finely granular white blood cells—*polynuclear leucocytes*—after fixation and staining, present a highly chromatic, deeply basophilic nucleus which varies greatly in form. Thus it may be indented, horseshoe-shaped, S-shaped, elongated and twisted upon itself, or separated into distinct lobes which are connected together by means of fine chromatic filaments. It is thus characteristically polymorphous, but in all its varying forms it is readily distinguishable from the mononuclear types by its extreme depth of stain, its intense *chromatophilia*.

The cytoplasm of these cells is considerable in amount and presents an extremely delicate reticulum, at the intersections of whose meshes are the minute neutrophile granules, which give the cell its finely granular appearance as seen in the freshly prepared specimen. The characteristic finely granular protoplasm and the polymorphous nucleus are the distinguishing peculiarities of these cells, the so-called "polynuclear neutrophile leucocytes."

P. Ehrlich in a series of communications announced that by coloring the leucocytes with various stains he was able to distinguish by their reaction, several types of granules. These he called (α) oxyphile or acidophile, which were deeply stained by eosin, acid fuchsin, etc.; (β) amphophile, which were stained both by eosin, and by dahlia and like dyes; (γ) basophile, which were stained deeply by dahlia, thionin, etc.; (δ) certain cells which neither after staining with eosin, etc., nor with dahlia, etc., could be made to show any granules other than the nodes of the cytoreticulum; (ϵ) neutrophile, which can be stained only by a due admixture of acid and basic dyes, as of fuchsin and methylen blue, or the so-called "triacid mixture" of Ehrlich.

The demonstration of these characteristics presupposed a division of dyes into three primary classes:

1. *Acid*—e. g., eosin, orange-G, acid fuchsin, aurantia, erythrosin.
2. *Basic*—e. g., methylen blue, dahlia, thionin, hematein.
3. *Neutral*—which are only formed by the interreaction of examples of each of the two preceding classes; the neutral dye is supposed to arise *de novo* in such mixtures, as a result of chemical reaction.

The application of such a classification of stains to other tissues than the blood has, however, been found to present considerable difficulties.

Centrosomes and mitotic figures have been repeatedly demonstrated in the polynuclear neutrophiles of the lower vertebrates and in those of human blood by Fleming,* Gulland,† and others. The meshes of their cytoplasmic reticulum—exclusive of the neutrophile granules—present a very slightly acidophile character, so that by overstaining in eosin, erythrosin, etc., the cytoplasm of these cells takes on a distinctly red tint. That this reaction is not due to the presence of hemoglobin is evidenced by the fact that red blood cells contained in the same specimen will invariably stain much more deeply with the acid dye than any of the leucocytes.



FIG. 81.—LEUCOCYTES
IN PROCESS OF
MITOSIS.

From the red marrow of a guinea-pig.
(After Demarbaix.)

The coarsely granular leucocytes of the blood—*eosinophiles*—possess a nucleus which presents the same polymorphous form

* Arch. f. mik. Anat., 1891.

† J. of Physiol., 1896.

and highly chromatic, deeply staining character as that of the polynuclear neutrophile type. Their cytoplasm differs, however, in that the intersections of the meshes of its cytoplasmic reticulum are occupied by very coarse spheroidal granules which are highly acidophile, and therefore stain deeply with such dyes as eosin, erythrosin, and acid fuchsin. The cytoplasm of these cells, exclusive of its specific granules, possesses a slightly acidophile nature similar to that of the polynuclear neutrophile type; this peculiarity can be readily demonstrated, as in the former case, by overstaining with acid dyes. Centrosomes and mitotic figures have also been repeatedly demonstrated in these cells.

Other coarsely granular cells—*basophile leucocytes*—possess a considerable rim of cytoplasm containing very coarse basophile granules. They are usually mono-, though frequently polynuclear. They form about 0.5 per cent of the white blood cells, and can therefore be disregarded as a normal constituent of human blood. In certain diseased conditions, notably in myelogenous leukemia, they appear in the circulation in considerable numbers.

None of the several forms of white blood cells possess a cell membrane, and in marked contradistinction to most other cells of the body the presence of a peripheral condensation of the cytoplasm (exoplasm) can not be demonstrated with any degree of certainty.

The several varieties of white blood corpuscles found in normal blood, with their prominent characteristics, may be summed up as follows:

1. *Small mononuclear leucocytes* or *lymphocytes*, with a non-granular basophile cytoplasmic rim of insignificant breadth, and a spheroidal deeply staining nucleus whose abundant chromatin is characteristically clumped to form even more deeply staining karyosomes. These cells are the smallest of the several types of leucocyte, and they form from 22 to 25 per cent of the white blood corpuscles in human blood.*

2. *Large mononuclear leucocytes* with a considerable rim of non-granular cytoplasm in which a slightly basophile reticulum can be demonstrated. These cells possess a faintly staining vesicular nucleus which is poor in chromatin; it is typically spheroidal in shape, but may be notched, indented, or even horseshoe-

* These figures are those originally given by Ehrlich. In infancy the relative percentage of small mononuclear leucocytes is often greatly increased (50 per cent) at the expense of the polynuclear neutrophils (40 per cent).

shaped. This is the largest of the several types of leucocyte: they form 2 to 4 per cent of the white corpuscles of the blood.

3. *Polynuclear neutrophile leucocytes* ("polymorphonuclear" neutrophiles, polynuclear leucocytes) possess a broad rim of cytoplasm, which contains fine neutrophile granules, and a deeply staining polymorphous nucleus consisting frequently of three or four ovoid lobes united by a delicate chromatin thread. These are relatively large cells: they form 70 to 72 per cent of the white blood cells, and are therefore the most abundant of the several types of leucocyte.

4. *Eosinophile leucocytes* (polynuclear eosinophiles, acidophiles, or oxyphiles) have a broad rim of cytoplasm with very coarse, highly acidophile granules, and a highly chromatic polymorphous nucleus which resembles that of the neutrophiles and consists usually of several distinct lobes united by chromatin threads. In relative size they are similar to the neutrophiles. Eosinophile cells form 2 to 4 per cent of the white blood corpuscles.

5. *Basophile leucocytes* ("mast-cells") are provided with a considerable cytoplasmic rim containing coarse basophile granules; they may be either mono- or polynuclear, the nucleus in either case not being richly supplied with chromatin. In size these cells resemble the neutrophiles. They are the least frequent of the several types of leucocytes, but form at least 0.5 per cent of the white blood cells.

Development of the White Blood Cell.—The primary origin of the embryonic white blood cells is still a matter of some obscurity. They make their appearance considerably later in fetal life than the red blood cells. According to Saxer,* the first white blood cells are derived by reproduction and differentiation of those same ancestral mesoblastic cells which at first form only red blood cells, but later the white cells as well. These primitive wandering cells gain admission to the blood vessels by their amoeboid activity. Kostianecki,* however, thinks that these ancestral cells are formed within the dilated portions of the primitive vessels, and that the earliest white blood cells are therefore formed within the vessel and probably stand in intimate genetic relation with the primitive endothelium.†

* Anat. Hefte, 1896.

† The recent studies of Beard have thrown some doubt upon the former conception. This observer finds that there are no leucocytes in the blood prior to the appearance of the anlage of the thymus. He also finds that in the earliest

In later fetal life, as in the adult, the formation of white blood cells takes place actively in all the lymphoid organs and tissues. Those cells which are found in the germinal centers of the lymphatic nodules are especially active; their cell reproduction is by mitosis, the daughter cell, according to Fleming, being of the lymphocyte type.

The presence of centrosomes and mitotic figures in all varieties of leucocytes, both in the adenoid tissues and under certain conditions in the blood as well, has been so constantly found as to indicate that this, rather than amitosis as was formerly supposed, is perhaps the only method of cell division by which white blood cells are reproduced. The same fact would indicate that each variety of leucocyte when once established is capable of reproducing itself.

As soon as leucocytes appear in the fetal blood current all of the several varieties can be distinguished. It is therefore doubtful if one variety can in any way be regarded as a more mature form than the other.

While in fetal life all varieties of leucocyte may be formed in any lymphoid organ, yet with the appearance of the bone marrow the formation of the granular varieties, eosinophiles, neutrophiles, and basophiles, appears to become most active in this tissue. It is possible that the marrow is the only tissue in which these cells are reproduced in adult life (Ehrlich). The mononuclear non-granular types—lymphocytes and large mononuclear cells—continue to be actively regenerated in the lymphoid organs, i. e., the lymphatic nodes, lymphatic nodules, and spleen.

The finding of large giant cells, megakaryocytes,—resembling the osteoclasts, but differing therefrom in that the former possess a single polylobar nucleus, whereas the osteoclast is multinuclear, each nucleus being of ellipsoid shape and of approximately equal size—in all hemopoietic tissues, has been taken to indicate

anlage of the thymus primitive leucocytes are formed by mitotic division of cells which are apparently derived from the epithelium of the gill clefts. Working independently, Nussbaum also found that the anlage of the thymus in fishes was derived from the epithelium of the primitive gill clefts. These observations would therefore indicate a possible ectoblastic origin for the leucocytes, and that the earliest cells of this type, as later in life, are derived from the lymphoid organs, and only by their characteristic nomadic tendency do they gain admission to the primitive blood vessels to be thereby distributed to distant portions of the fetal body. These observations, however, lack further confirmation.

a relation between these giant cells and the formation of blood corpuscles. It seems probable, however, that these cells are more concerned with degenerative processes, e. g., the absorption of the nuclei of erythroblasts, than with the regeneration of blood cells.

THE BLOOD PLATELETS (*third corpuscles, blood plaques or plates, hematoblasts of Hayem, thrombocytes*).—The blood platelets are minute ovoid or ellipsoid, colorless, granular bodies much smaller than the red blood cells. They vary

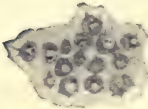


FIG. 82.—A GROUP OF BLOOD PLATELETS, FROM THE HUMAN BLOOD.

Very highly magnified.
(After Eisen.)

considerably in size, but are mostly from 2 to 4 μ in diameter. Blood platelets can be demonstrated in living blood, and therefore form a constant structural element of the blood. It is found that after drawing blood from the vessels these elements increase rapidly in number for a short period, and as their number is subject to constant variation from other causes it is impossible to assign them a definite numerical

relationship to the red and white blood cells. The number of blood platelets has been variously estimated at from 200,000 to 600,000 per cubic millimeter.

The blood platelets present a remarkable tendency to collect into masses containing considerable numbers of these elements. It is in the vicinity of such accumulations that the first fibrils of fibrin make their appearance during coagulation, and for this reason the platelets have been assumed to bear an important relation to the production of fibrin in shed blood.

Blood platelets as a rule present but little appearance of finer cell structure. They are usually non-nucleated globular masses of finely granular protoplasm which have a slight affinity for most basic dyes and are deeply stained by gentian violet, thionin, etc. Under favorable conditions they can be observed to execute amœboid movements, sending out long and very slender protoplasmic processes. Nuclei can also be demonstrated in at least a portion of the platelets, and some observers (Deetjen,* Kopsch†) are inclined to consider them as being typically nucleated blood cells.

The development of the platelets is still obscure. They were formerly supposed, because of their basophile properties, to be products of degeneration or of disintegration of the white blood corpuscles. This theory has not received further corroboration.

* Arch. f. path. Anat., 1901.

† Anat. Anz., 1901.

On the other hand, the platelets undoubtedly stand in relation to the red blood cells, since the latter can frequently be seen in the apparent act of extruding from their substance globular elements closely resembling the platelets in appearance and staining reaction.

More or less apparent confusion of the subject has arisen from the supposed analogy of the true blood platelets of human blood with certain other structures found in the blood of the lower vertebrates, especially the "spindle-cells" of amphibians. Eisen* has cleared the matter considerably by demonstrating the presence in batrachian blood of true platelets in addition to the characteristic "spindle-cells." He has also shown that in at least one species the true platelets represent the survival of the extruded centrosome and archoplasm of the red blood cells. These platelets he finds to be at first nucleated and amoeboid (*plasmocytoblasts*); by mitotic division the plasmocytoblasts of Eisen produce platelets which lose their nucleus and in every way resemble the true blood platelets (*plasmocytes* of Eisen). It is thus possible that the nucleated platelets of mammalian blood are premature types, and that the true platelets are genetically related to the disappearance of the nuclei of the erythrocytes with the possible survival of certain of its achromatic portions.

OTHER ELEMENTS OF THE BLOOD.—Under certain conditions the blood contains a considerable proportion of *fat* globules. These are most abundant a few hours after a hearty meal, especially if it contain an undue proportion of fatty food. The fat globules which are thus found are of small size and float free in the plasma.

In addition to fat the blood has been found to contain other fine granular particles which mostly represent the detritus from disintegration of the blood cells. The "*blood-dust*" and the "*hemoconia*" of Müller are of this nature.

Plasma and Serum.—*Plasma* is a clear colorless fluid in which the formed elements of the blood are suspended. It is therefore devoid of histological structure.

Serum is likewise of a fluid nature, but differs histologically from the plasma in that it contains in solution or suspension the products of that disintegration of blood cells which is concomitant with coagulation. Serum is therefore of a faint amber color from the presence of hemoglobin in solution, and in addition to

* Proc. Calif. Acad. of Sc., 1897; also, J. of Morphol., 1899.

the corpuscular clot it contains fragments of red and white corpuscles and of fibrin.

Fibrin.—If a specimen of freshly drawn blood be allowed to remain in the field of the microscope, it will be noticed, after

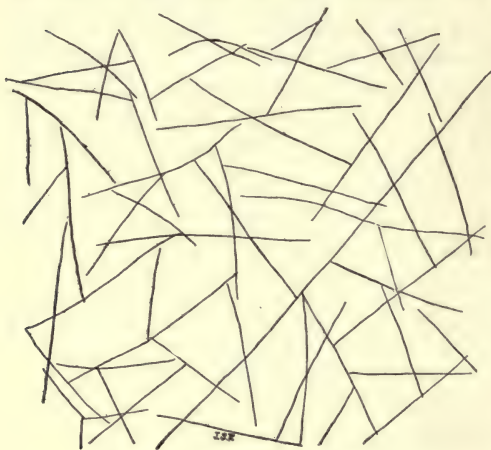


FIG. 83.—FIBRILS OF FIBRIN.

Drawn from the same preparation as is represented in Fig. 74, but only after an interval of several hours. $\times 1065$.

some time, that fine colorless fibrils appear within the spaces between the corpuscular elements. This formation of fibrin takes place first in the more exposed portions of the specimen at the edge of the cover glass, but in course of time extends throughout the entire specimen. The fine filaments thus formed produce a dense network of interlacing fibrils. This fibrin net eventually contracts, drawing with it the

corpuscles, which are thus crowded into groups to form with the fibrin the denser clot, the fluid serum being expressed into the interval between adjacent masses of clot.

Careful observation of the earliest formed fibrils of fibrin will show that they can be first recognized about the margins of the groups of blood platelets and in relation to the white blood corpuscles. This appearance is taken to indicate a close physiological relation between these elements and the formation of fibrin.

Hemoglobin.—The coloring matter of the blood is a compound of iron with a globulin. This hemoglobin is held either in solution or in loose chemical combination by the cytoplasm of the red blood corpuscles. It escapes from these cells after rupture of their limiting membrane and is then capable of being crystallized in the form of minute brownish-yellow prisms.

The color of the blood is entirely due to the presence of hemoglobin in its red cells. When examined by transmitted light, solutions of hemoglobin—and likewise the red blood corpuscles—have a faint greenish-yellow or amber color; by reflected light

they possess the familiar crimson tint of freshly drawn blood. In thin layers solutions of hemoglobin are quite transparent, in thicker layers they become more and more opaque.

Various crystalline and amorphous substances may be obtained by decomposition of hemoglobin. The iron of the coloring matter may be thus obtained in the form of *hematin*, a soluble amorphous compound of a brownish-red color. If hematin is combined with hydrochloric acid the chlorid of hematin, *hemin*, is produced. Hemin occurs in deep brownish-red crystals which differ somewhat according to the animal species from which they are obtained; those of human blood take the form of triclinic plates.

Hemin crystals derive a certain importance as a forensic test for the presence of blood, and they may be obtained from old and dried-up specimens as readily as from fresh blood. The hemin crystals obtained from human blood, however, are identical with those from the blood of other mammals.

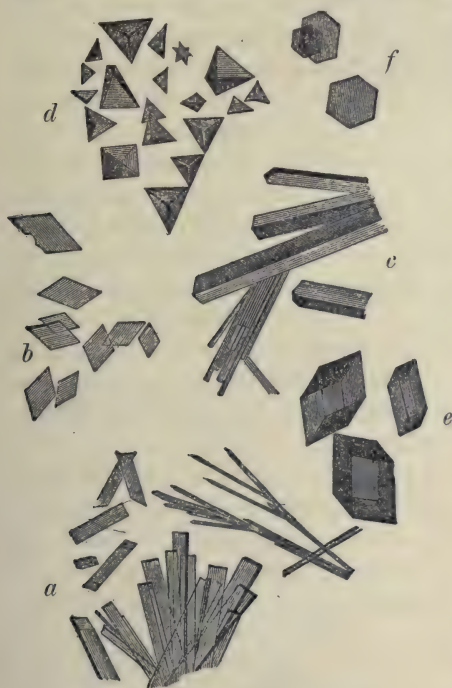


FIG. 84.—HEMOGLOBIN CRYSTALS.

a and *b*, from human blood; *c*, from the cat; *d*, from the guinea-pig; *e*, from the hamster; *f*, from the squirrel. (After Ranvier.)



FIG. 85.—CRYSTALS OF CHLORID OF HEMATIN OR HEMIN.

(After Ranvier.)

When extravasations of blood occur within the tissues of the body the coloring matter is frequently deposited as *hematoidin*, an iron-free derivative of hemoglobin which forms stellate groups of yellowish needle-like crystals.

CHAPTER VII

THE VASCULAR SYSTEM

THIS system includes the heart, arteries, capillaries, veins, and lymphatic vessels. These structures form a continuous set of branching tubes, which convey the blood from the heart, through the arteries and capillaries, and back again through the veins to the heart. In the capillaries a portion of the blood plasma transudes into the tissue spaces, where it forms the "tissue juices," and from which it is returned to the blood by the lymphatic vessels, the terminal branches of which empty into the subclavian veins.

This entire vascular system is completely lined by a single layer of flattened epithelial cells, *endothelium*, which are united edge to edge by an intercellular cement substance, to form a continuous membrane throughout the entire system. The blood vessels include the arteries, capillaries, and veins, and these, together with the heart, will form the subject of the present chapter; the lymphatic vessels will be described in connection with the lymphatic system.

ARTERIES.—The arteries convey the blood from the heart to all the tissues of the body. They are therefore almost universally present, but vary in size from the aorta down to minute unnamed vessels of microscopic caliber. They are divisible, according to size, into the large, medium sized, and small arteries, the arterioles, and what may be termed the arterial capillaries, or "precapillary arteries." The large arteries include only the aorta and the largest of its immediate branches; the medium-sized arteries comprise nearly all the remaining named arteries of the body; small arteries, arterioles, and precapillary arteries include those unnamed arteries which are to be found in nearly all of the organs and tissues of the body.

A medium-sized artery will be first described, as presenting the typical arterial structure. Such a vessel consists of three coats:

1. The internal coat—*tunica intima*.
2. The middle coat—*tunica media*.
3. The external coat—*tunica adventitia*.

The internal coat, *tunica intima*, presents three layers, the innermost being the layer of endothelial cells, the outermost a layer of elastic tissue, the fenestrated coat of Henle, or internal elastic membrane; between these is a delicate fibrous membrane, which constitutes the middle layer.

The endothelium comprises only a single layer of flattened or squamous cells, placed edge to edge to form a continuous membrane of simple pavement epithelium. These cells are irregularly polygonal in outline, and are

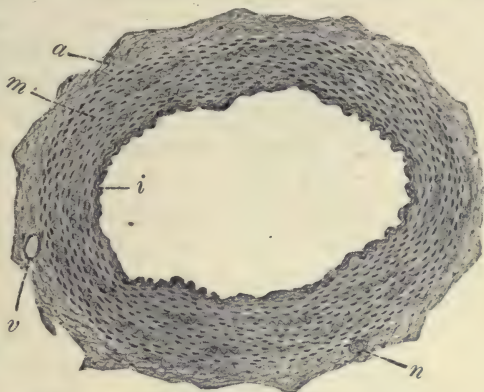


FIG. 86.—A SMALL ARTERY FROM THE CONNECTIVE TISSUE OF THE ANTERIOR CERVICAL REGION OF MAN.

a, tunica adventitia; *i*, tunica intima; *m*, tunica media; *n*, a small non-medullated nerve trunk; *v*, a minute venule. Hematein and eosin. $\times 370$.

somewhat elongated in the direction of the axis of the vessel. They are loosely attached to the elastic membrane by the middle layer of fine fibrillar connective tissue, in whose ground substance small branching connective tissue cells are found. The thickness of this connective tissue layer varies proportionately to the size of the vessel.

The *internal elastic membrane* is a layer of elastic tissue, consisting of an intimately united fibrous mass, which completely encircles the artery. In the smaller vessels the elastic fibres of this layer form only a reticulated structure, but in the larger arteries they are so abundant and so closely interwoven as to form a complete membrane, which can be readily stripped from the subjacent tissue. If the membrane thus prepared is examined microscopically, it will be found to present numerous small openings at points where the elastic tissue is deficient. It is this appearance which led to its description as a "fenestrated membrane." The internal elastic membrane is intimately united to the tunica media, upon which it rests; in fact, it may perhaps be better considered as the innermost layer of this tunic, for, in the larger arteries, e. g., the aorta, it can only with difficulty be distinguished from the adjacent layers of elastic tissue which form a large portion of the tunica media of these vessels.

The *tunica media*, or middle coat, contains smooth muscle, sheets of elastic tissue, and a very delicate fibrous connective tissue. The proportion of these elements present in any given artery varies with the size of the vessel. Muscular tissue usually predominates, but in the larger arteries elastic tissue is so abundant as to appear quite in excess of the muscular; in the smaller arteries, however, the muscular tissue is by far the more abundant.

The smooth muscle fibres are circularly disposed in the wall of the vessel; they are short, of irregularly serrated outline, and are intimately united with one another. Quite frequently the muscle fibres possess short branches which interdigitate with those of neighboring fibres. In the larger vessels they are arranged in

layers which alternate with the sheets of elastic tissue. Small bundles of longitudinal smooth muscle fibres are occasionally found in the outer portion of the *tunica media*.

The elastic tissue of the middle coat is disposed in membranous sheets which, in the larger vessels, are embedded in a fine fibrillar connective tissue. In these vessels, also, the fibro-elastic membranes thus formed alternate with the layers of smooth muscle, throughout the entire thickness of the *tunica media*. In consequence of the relaxation of the normal arterial tone and the contraction of the muscular wall in rigor mortis, as seen in the usual preparations, these elas-

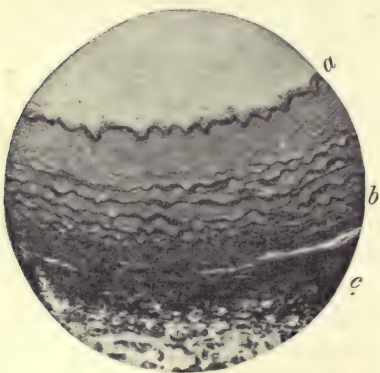


FIG. 87.—THE EXTERNAL CAROTID ARTERY OF A CHILD.

a, tunica intima, the internal elastic membrane is prominent; *b*, tunica media, containing smooth muscle and several wavy layers of elastic tissue; *c*, tunica adventitia, containing many transversely and obliquely cut elastic fibres and much wavy connective tissue. Photo. (After Magrath.)

tic layers, as well as the internal elastic membrane, are thrown into wavy folds.

The external coat, *tunica adventitia*, consists chiefly of fibrous connective tissue. Relatively few elastic fibres occur in this coat, and these for the most part lie in its inner portion, adjoining the *tunica media*. In the larger arteries, when especially abundant, the elastic fibres form an incomplete layer, which may be termed the *external elastic membrane*. Like the internal elastic membrane,

this layer might well be considered as belonging to the tunica media, of which coat it would then form the outermost stratum.

The white fibres of the tunica adventitia are disposed in dense interlacing bundles, to form a firm, unyielding coat. At the periphery of the artery the connective-tissue bundles of the adventitia intermingle with those of the adjacent areolar connective tissue, in which the blood vessels are nearly always embedded, hence the outer boundary of this coat is usually more or less ill-defined.

The fibrous bundles of the adventitia are disposed somewhat obliquely or diagonally about the artery, thus forming a closely felted connective-tissue network. Small blood vessels, both arteries and veins (*vasa vasorum*), and minute nerve trunks with occasional ganglia, occur in this coat. From these *vasa et nervi vasorum* capillaries and fine nerve fibres are distributed to the muscular coat. No blood vessels are found in the tunica intima.

General Characteristics of the Arterial Wall.—The tunica media is almost invariably the thickest of the arterial coats. In the larger vessels the adventitia is often of nearly equal thickness, but in the medium sized and small vessels it is much thinner. The arterial wall, as a whole, also, is very thick as compared with the lumen of the vessel, and is much thicker than that of a vein of corresponding size.

The wall of the larger arteries is relatively thinner as compared with the lumen than is the case with the smaller arteries; in these latter vessels the thickness of the arterial wall often exceeds the diameter of their lumen. In certain small arteries, e. g., those of the liver, even this ratio is exaggerated, the excess of muscular tissue in these vessels resulting in a breadth of wall which may be as much as two or three times that of the lumen.

The arterial wall contracts firmly in rigor mortis, hence the



FIG. 88.—TRANSECTION OF THE WALL OF THE AORTA OF A CHILD.

The elastic tissue is deeply stained. 1, tunica intima; 2, tunica media; 3, tunica adventitia. Weigert's elastic stain and picro-fuchsin. Photo. $\times 64$.

arteries after death contain but little blood, and, because of the density of the tissues which compose their wall, these vessels retain, as a rule, their cylindrical form.

The Large Arteries.—The largest arteries differ from the medium-sized type in the excess of elastic tissue and relative deficiency of muscle in their media, the extreme thinness of their adventitia, and the relative thinness of their wall, as a whole, when compared with their lumen. Elastic tissue is especially abundant in all of these vessels; in the media it exceeds in volume the muscular tissue, in the adventitia it forms a dense network of elastic fibres.

The adventitia of the largest arteries is extremely thin, that of the thoracic aorta being not much thicker than its fibrous tunica intima; this coat, therefore, forms but a small portion of the vascular wall in vessels of this type. In the medium-sized vessels, e. g., the iliac arteries, the tunica adventitia more nearly approaches the media in thickness.

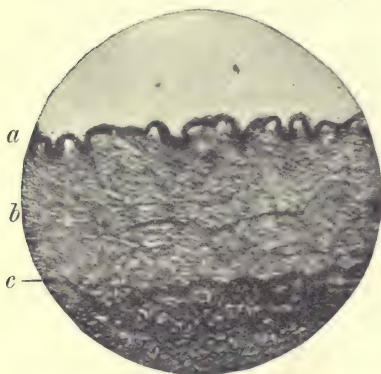


FIG. 89.—TRANSECTION OF THE CELIAC AXIS OF MAN.

a, tunica intima with a prominent internal elastic membrane; b, tunica media, consisting chiefly of smooth muscle; c, external elastic membrane in the inner portion of the tunica adventitia. Photo. (After Magrath.)

In the **small arteries** the elastic tissue is relatively decreased and the smooth muscle noticeably increased. The tunica intima of these vessels is thin, and is limited externally by an internal elastic membrane, which stands out prominently because of the relative deficiency of elastic tissue in the tunica media.

In the tunica media of these vessels the plates of elastic tissue which characterize the larger arteries are scarcely to be found. This coat in the small arteries contains very little tissue other than smooth muscle.

The external elastic membrane is indistinct, and the adventitia is not more than one-half to two-thirds as thick as the tunica media.

The **arterioles** possess a relatively thicker wall than any other vessel of the arterial system. Their tunica intima is thin, but little fibrous tissue being contained within it, and the internal

elastic membrane is represented only by a very incomplete layer of elastic fibres. The tunica media of the arteriole forms two-thirds to three-fourths of its wall, and consists almost entirely of firmly united smooth muscle fibres. The adventitia, much thinner than the media, contains bundles of white fibres and delicate interlacing elastic fibrils.

The smallest arterioles pass into what may be termed the **precapillary arteries**. In these minute vessels the wall consists of scarcely more than the endothelial lining, about which is an incomplete layer of circular muscle fibres, interspersed with occasional white fibrous and elastic fibres. On approaching the capillaries the endothelial tube is gradually laid bare. It is the smooth

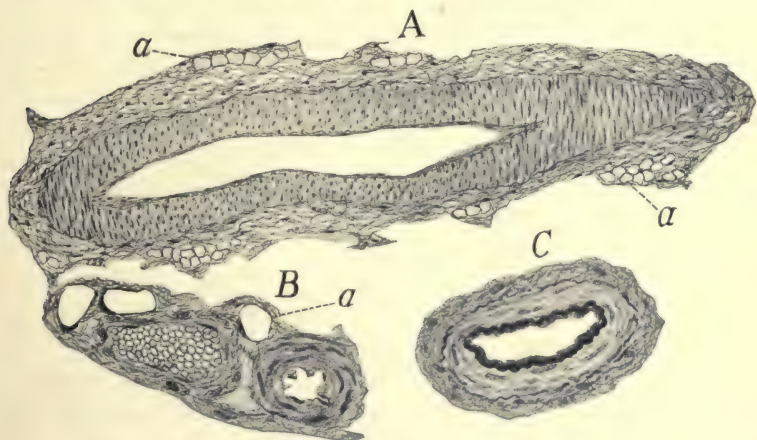


FIG. 90.—A GROUP OF SMALL BLOOD VESSELS.

A, small artery obliquely cut; *B*, arteriole and venule, the latter filled with blood; *a*, fat cells. *A* and *B* are from the connective tissue of the anterior cervical region. Hematein and eosin. *A*, $\times 110$; *B*, $\times 550$. *C*, a small arteriole near the descending aorta of man; the internal and external elastic membranes are rendered distinct by the stain. Hematein, Weigert's elastic tissue stain, and picro-fuchsin. $\times 550$.

muscle which is the last of the tissues to disappear from the arterial wall, whereas beyond the capillaries it is the fibrous tissues which are first added to the endothelial tube to form the wall of the smallest venules (Fig. 94).

Comparison of Large and Small Arteries.—The larger arteries are typically elastic, the smaller typically muscular. In the larger vessels the elastic tissue forms about one-half of the entire wall; toward the smaller arteries this tissue progressively diminishes until, in the arterioles, it is limited to an incomplete internal

elastic membrane, the homologue of the complete elastic coat or fenestrated coat of Henle, which is found only in larger vessels.

The smooth muscle, on the other hand, increases in *relative* amount from the larger to the smaller arteries. While in the largest vessels it forms not more than one-third, in the arterioles it represents about three-fourths of the arterial wall.

In the largest arteries the adventitia is relatively very thin. That of the medium sized vessels is somewhat thicker, and the ratio of connective tissue as found in the wall of these vessels remains fairly constant down to the arterioles. In the wall of the precapillary arteries connective tissue is very scanty.

CAPILLARIES.

— The capillaries are minute tubes, 5 to 13μ in diameter, which, in nearly all the tissues of the body, connect the arteries with the veins. Their wall



FIG. 91.—THE CAPILLARY NETWORK CONNECTING AN ARTERIOLE AND VENULE OF THE OMENTUM OF A YOUNG RABBIT.

The blood vessels have been injected. The discolorations at *l* and *l* are due to the presence of lacteals beneath the endothelium; at *l'* and *l'* these are surrounded by the capillary network. *a*, arteriole; *v*, venule. Considerably magnified. (After Ranvier.)

is formed by a layer of endothelial cells which on the one hand is continuous with the endothelial lining of the arteries, on the other hand with that of the veins.

As a rule there are neither muscle fibres nor connective tissue in the wall of the true capillaries; occasionally, however, very fine isolated circumferential elastic fibres encircle the endothelial tube. In the minute arterioles and venules, which are about to terminate in or take origin from the true capillaries and which have been described as precapillary arterioles and venules, a very thin layer of muscle fibres or of connective tissue is added to the endothelial wall of the capillary. On the arterial side the muscle is the first tissue to be thus added, on the venous side the fibrous connective tissue is the first to appear.

The endothelium of the capillary wall consists of flattened plate-like cells which are joined edge to edge by cement sub-



FIG. 92.—CAPILLARY VESSEL OF THE FROG'S MESENTERY.

Treated with nitrate of silver to show the outlines of the endothelial cells. Highly magnified. (After Ranvier.)

stance. These cells are somewhat elongated in the axis of the vessel, the shape of the cell, as in the arteries and veins, depending upon the size of the vessel—the smaller the vessel the more elongated its endothelial cells. The margins of these cells are extremely irregular, hence they present a wavy or serrated outline.

Although the endothelial cells of the capillary wall appear to be firmly united to one another, yet they are capable of being separated sufficiently to permit the ready passage of white blood cells through the capillary wall, by means of diapedesis. The capillary wall does not appear to be an inactive factor in this process, for inert pigment granules may also penetrate the wall of these vessels, the endothelial cells immediately closing the aperture which is thus formed. Nevertheless, purely mechanical means, e. g., increased blood pressure, appear also to favor this process. The openings which are formed between the endothelial cells by the process of diapedesis are very transitory; they are almost immediately closed by the activity of the endothelium. Such transitory breeches of the capillary wall are termed *stigmata*.

The capillaries branch and anastomose with one another to form networks, the outlines of whose meshes vary according to the tissue in which they occur. In such fibrous tissues as muscle

and nerve they form elongated meshes whose long axes are parallel to those of the muscle or nerve fibres; in the looser, more areolar tissues they form large meshes of irregular form; while in the capillary membranes, as in the walls of the pulmonary alveoli, they are disposed in a close net the diameter of whose meshes scarcely exceeds that of the capillaries.

With but few exceptions capillaries occur in all the tissues of the body. In epithelium and in cartilage there are no blood vessels of any kind, and in the splenic pulp it is doubtful if true capillaries occur. In certain tissues large vascular spaces occur, which are comparable to the capillaries in that their wall consists of scarcely more than the endothelial tube, but which differ from the true capillaries in the extreme size of their lumen. These vessels have been described by Minot*

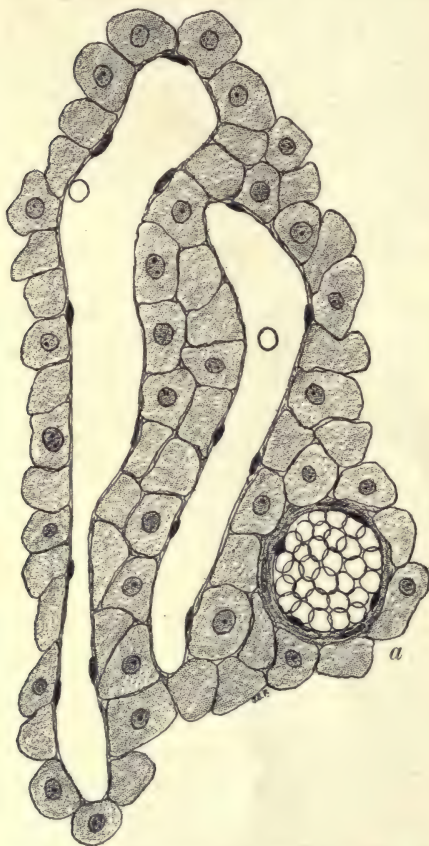


FIG. 93.—TWO SINUSOIDAL VESSELS FROM THE MEDULLA OF THE HUMAN ADRENAL.

Each contains the outline of a single red blood cell for comparison of size. At *a*, a small vein is shown; it is filled with blood and possesses a much thicker wall than that of the sinusoids. Hematein and eosin. $\times 410$.

as *sinusoids*. They are found in the erectile tissues, adrenals, coccygeal gland, parathyroids, and heart, in the maternal placenta, and in the fetal liver, pronephros, and Wolffian body.

*J. Bost. Soc. of Med. Sc., 1900.

VEINS.—The blood having passed the capillaries, enters the smallest radicals of the venous system, the precapillary venules, and passes thence through the venules to the larger veins. The progressive increase in the caliber of these successive vessels is accompanied by a corresponding increase in the thickness of their wall. Thus, while the endothelial tube alone composes the capillary wall, the endothelium of the precapillary venule is encircled by a delicate connective tissue membrane. In the venule occasional smooth muscle fibres are added to the wall of the smaller vessel, and in the vessels of this caliber the fibrous tissues have been so increased that the vascular wall, as in the artery, can be said to possess three coats.

The wall of the **precapillary venule** consists of the endothelial lining, which is surrounded by a very delicate connective tissue membrane in which are very few elastic and white fibres.

In the **venule** the tunica intima consists of little more than the endothelial lining. Its media and adventitia are not as yet distinctly differentiated, the former being distinguished only by the incomplete layer of circularly disposed smooth muscular fibres. The extremely thin adventitia is composed almost wholly of white fibres, the greater part of which are circularly disposed. Very few elastic fibres occur even in vessels of this size.

In the **small veins** the three coats are fairly distinct, the vascular wall being, however, much thinner than in the artery of corresponding size.

The endothelium of the tunica intima is supported by a very delicate connective-tissue membrane which as yet contains but few elastic fibres.

The tunica media consists of a thin layer of circularly arranged smooth muscle fibres intermingled with a delicate fibrous tissue; elastic fibres are relatively scarce.

The adventitia, though considerably the thickest of three coats, is as yet a thin membrane. It consists of fibrous connective

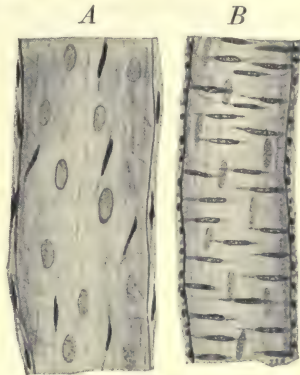


FIG. 94.—PRECAPILLARY ARTERIOLE AND VENULE.

The lighter nuclei are those of the endothelium. The darker nuclei in the venule are in connective tissue cells; in the arteriole they are in the muscle cells. *A*, venule; *B*, arteriole. Partly diagrammatic. Highly magnified.

tissue, elastic fibres being scarcely demonstrable except by means of the specific stains for this tissue.

The wall of the **larger veins** closely resembles that of the corresponding artery, except that the venous wall is much thinner and contains far less elastic tissue. The tunica intima of the medium and large veins presents a lining endothelium, a thin layer of delicate connective tissue fibres, and an incomplete internal elastic membrane. The last named is never so prominent as in the artery.

The tunica media contains smooth muscle fibres, the most of which are circularly arranged. A somewhat smaller proportion of delicate connective tissue completes this coat.

The adventitia of the larger veins consists of interlacing bundles of dense white fibres, among which is a network of fine elastic fibres. Occasional small bundles of longitudinal smooth muscle fibres occur in the adventitia of the largest veins. In these vessels also, a very incomplete external elastic membrane may be demonstrated by the specific stains for elastic tissue.

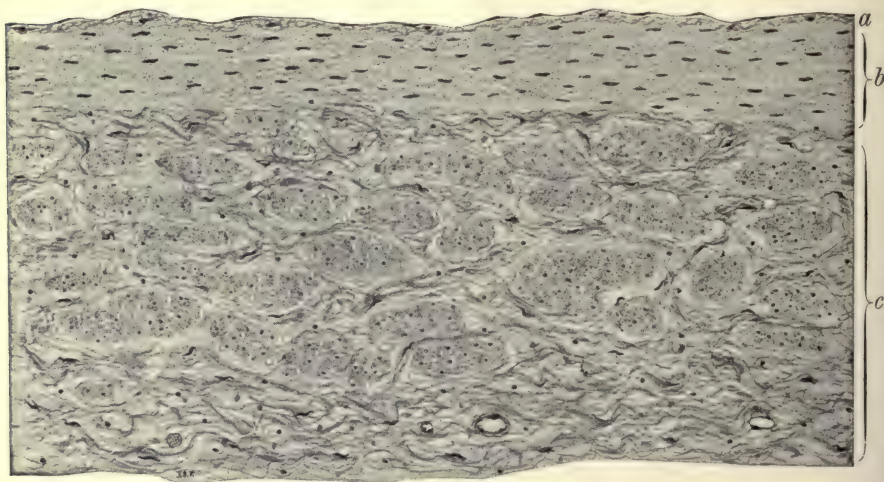


FIG. 95.—TRANSECTION OF THE WALL OF THE HUMAN VENA CAVA.

a, tunica intima; *b*, tunica media; *c*, tunica adventitia. The inner portion of which contains numerous bundles of longitudinal smooth muscle fibres which have been cut across. Hematein and eosin. $\times 90$.

Nerve fibres and minute blood vessels, *vasa vasorum*, occur in this coat and distribute their terminal branches to the two outer coats of the vessel. The intima of the vein, as in the artery, is non-vascular.

In certain tissues the veins present noticeable **departures from the typical structure**. *Longitudinal muscle fibres* are found in many of the larger veins of the abdominal and thoracic cavities.

The *adrenal veins* contain, almost exclusively, longitudinal muscle fibres, and in the *renal* and *phrenic veins* and the *vena cava* these fibres form the greater portion of the tunica adventitia.

In the *pulmonary veins* the circular muscle fibres are highly developed, the tunica media of these veins almost equaling in thickness that of the corresponding pulmonary artery. As in other large veins, however, elastic tissue is notably deficient in the tunica media of the pulmonary vessels.

The tunica media of the largest veins, e. g., the vena cava, contains much fibrous and considerable elastic tissue, the latter often forming incomplete membranous layers, which alternate with the muscle, as in the arteries. Such structure is, however, limited to the very largest of the veins.

The *cranial veins* are conspicuous for the almost entire absence of muscle from their walls, the large meningeal sinuses being surrounded by a dense fibrous coat derived from the dura mater, and lined by the usual endothelium.

The *venous spaces* of the erectile tissues have already been mentioned as presenting to some extent the sinusoidal type of structure, these large venous cavities possessing an extremely thin wall, in structure scarcely more than an endothelial lining. The afferent artery projects into the broad vascular lumen, from which the efferent vein makes its exit.

Comparison of the Larger and the Smaller Veins.—Comparing the larger with the smaller veins, the excess of elastic and muscular tissue in the former is most noticeable: In the absence of specific stains, elastic tissue can scarcely be recognized in the venules and smaller veins. In the medium sized vessels it is scanty, but is present in considerable quantity in the largest vessels.

The precapillary veins and venules contain scarcely any smooth muscle. This tissue becomes more distinct in the small veins and steadily increases proportionately to the size of the vessel; in the largest veins it is again relatively deficient.

Comparison of the Vein with the Artery of Corresponding Size.—The lumen of any given artery is always much smaller than the total lumen of its venæ comites, the ratio being about one to three. Hence, of any two vessels in close proximity to each other,

the vein would more likely possess the larger caliber; the artery, on the hand, would have the thicker wall.

As compared with the arteries, the veins are notably deficient in elastic and muscular tissue. In the wall of most veins the white fibrous is in excess of all other tissues. For this reason the adventitia is almost invariably the thickest of the three coats of the vein, whereas in the artery the media is always the thickest coat.

The internal elastic membrane, which can be readily recognized even in the smaller arteries, is limited to the large veins. Alternating layers of elastic and muscular tissues are to be seen even in the medium sized arteries, but this arrangement is likewise confined to the largest of the veins.

The wall of the vein as a whole is much thinner in proportion to its lumen than that of the corresponding artery; it is also less

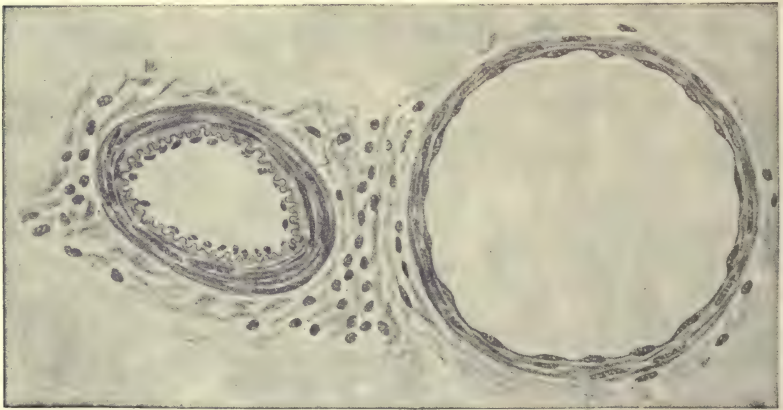


FIG. 96.—TRANSECTION OF AN ARTERIOLE AND VENULE.

× 250. (After Schäfer.)

rigid. For this reason the wall of the vein is much more likely to collapse after death than is the thicker and more rigid arterial wall. Because of the preponderance of muscle in the wall of the artery its contraction in rigor mortis is more powerful than that of the vein; the vein therefore is apt to be distended with blood while the artery contains but little. A certain number of blood cells can usually be found in almost any type of blood vessel.

Valves occur at intervals of considerable length along the course of the larger veins. These are not found in the arteries. Each valve consists of one, two, or more crescentic folds or redupli-

cations of the tunica intima between which is a slightly increased amount of connective tissue. The valves therefore are suspended free in the lumen of the vessel and are covered on either side with a layer of endothelium which is continuous with that lining the vein.

The fact should be borne in mind that it is because of their relative infrequency that valves are not often met with in those transections of the smaller veins which are seen in nearly all microscopical preparations.

HEART.—The wall of the heart consists of interlacing bundles of cardiac muscle fibres, the *myocardium*, which are covered externally by the *epicardium*, a serous membrane which forms the visceral layer of the pericardium. Internally the muscular wall of the heart is lined by the *endocardium*, which resembles the serous membranes in that it consists of pavement endothelium supported upon a layer of connective tissue. The endocardium lines all the cavities of the heart, and its endothelium is directly continuous with that of those arteries and veins which are connected with the cavity of the heart. Thus the entire vascular system—heart, arteries, capillaries, lymphatics, and veins—may be said to be lined by an uninterrupted sheet of pavement epithelial cells, the *endothelium*.

Myocardium.—The muscle cells of the myocardium are so disposed as to form long fibrous bundles which by their figure-of-8 arrangement are interwoven with one another to form a dense interlacing mass of muscle bundles. The structure of these cardiac muscle cells has already been described. Because of the irregularity of their disposition, transections of the cardiac wall present sections of muscle fibres which have been cut in every conceivable direction.

Between the muscle fibres is a very delicate framework of fibrous connective tissue, the *endomysium*, which surrounds the muscle fibres and supports the abundant capillaries, arterioles, and venules, with which they are supplied. The proportion of connective tissue in the normal myocardium as compared with the muscle is, nevertheless, very small.

In certain portions of the myocardium connective tissue is more abundant. Thus it is slightly increased in the vicinity of the endocardium, in the papillary muscles, and near the bases of the cardiac valves. At the surface of the heart, beneath the epicardium, and especially in the various grooves on the surface of

the heart, the connective tissue is still more abundant, and may contain groups of fat cells. It is through these accumulations of connective tissue that the larger blood vessels are distributed to the myocardium.

Epicardium.—The epicardium, like the other serous membranes, consists of a layer of pavement cells, so joined edge to edge as to form a complete

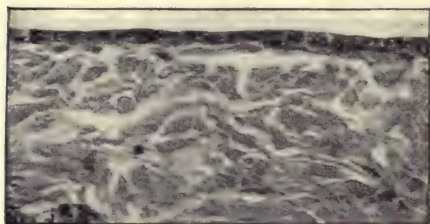


FIG. 97.—THE PARIETAL LAYER OF THE PERICARDIUM OF A CHILD.

a, endothelium; *b*, connective tissue. Hematein and eosin. Photo. $\times 500$.

endothelial coat. Here and there the endothelium presents small openings at the angles between its cells; these stomata are surrounded by minute, finely granular cells and are connected with the lymphatic vessels.

The endothelium of the epicardium is supported upon a thin layer of dense areolar tissue in which are many small blood vessels and lymphatics. Fibres from the deeper surface of this layer are prolonged into the myocardium to become continuous with its endomysial connective tissue. The larger of these connective tissue trabeculae accompany the branches of the larger arteries and veins which are distributed to the muscular wall of the heart.

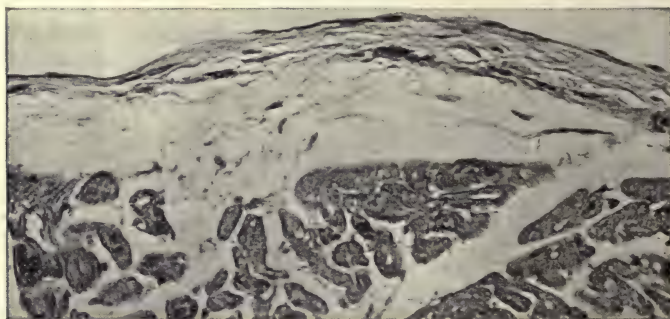


FIG. 98.—THE ENDOCARDIUM.

From the ventricular wall of the heart of man. Hematein and eosin. Photo. $\times 469$.

Endocardium.—The endocardium consists of a lining membrane of polygonal endothelial cells supported upon a thin layer

of delicate fibrous connective tissue. In this membrane is a network of elastic fibres. The endothelium of this membrane is continuous with that of those blood vessels which open from the cavities of the heart. Its connective tissue also forms a continuous layer with that of the tunica intima of these vessels: in fact, the three coats of the cardiac wall—endocardium, myocardium, and epicardium—might well be compared with the corresponding three coats of the arterial and venous walls—the intima, media,

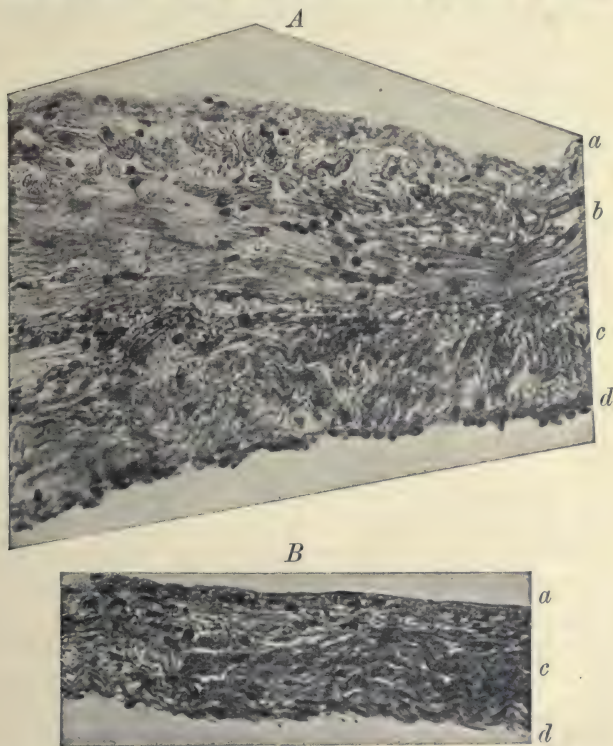


FIG. 99.—RADIAL SECTIONS OF THE MITRAL VALVE, FROM THE HEART OF A MAN.

A, from the base of the valve showing the extension into it of cardiac muscle fibres from the wall of the heart; *B*, from the mid-region of the valve. *a*, auricular endocardium; *b*, muscle fibres; *c*, dense fibrous tissue; *d*, ventricular endocardium. Hematein and eosin. Photo. $\times 800$.

and adventitia. In either organ, the inner coat consists of a lining membrane of endothelium, and a supporting membrane of connective tissue; muscle in large part composes the middle coat, while the outer coat is typically a connective tissue layer.

Valves.—At the cardiac orifices the entire thickness of the endocardium is folded upon itself to form a double layer, between the folds of which an intervening stratum of dense fibrous tissue is inserted. These endocardial folds are the cardiac valves. The number and shape of their cusps are dependent upon the location. The semilunar valves of the aortic and pulmonary orifices consist of three crescentic endocardial folds; at the auriculo-ventricular orifices the tricuspid valve consists of three large cusps, the mitral of two, together with an equal number of small intervening folds of the endocardium.

The margin of the valvular cusp is extremely thin; just within the margin, however, the central mass of dense fibrous tissue is somewhat thickened to form, in each cusp, a dense rim which during valvular closure secures the firm and accurate approximation of the free margins of adjacent cusps. At the apex of the valvular cusp, where the adjacent fibrous margins of the valve meet, the dense connective tissue, particularly in the semilunar valves, is considerably thickened to form the corpus Aurantii. These corpora, in the aged, are frequently subject to calcareous infiltration.

Muscular fibres are frequently continued from the adjacent cardiac or arterial wall into the dense fibrous tissue at the base of the valve. The base of the valve is also surrounded by a ring of fibrous tissue, the *annula fibrosa*, whose interlacing bundles are so closely packed as to give them an almost cartilaginous feel. At the auriculo-ventricular orifices, these fibrous rings are continuous with the auriculo-ventricular septum, from which the muscle bands of the myocardium take their origin.

Chordæ tendineæ.—These are firm, unyielding cords, composed of parallel bundles of dense white fibres, and covered with a very thin endocardium continuous with that of the ventricular wall and cardiac valve. These fibrous bands unite the apices of the papillary muscles to the ventricular surfaces of the mitral and tricuspid valves. At the apex of the papillary muscle the fibrous bundles of the chordæ intermingle with the muscle fibres, and are continued into the endomysial connective tissue, which is especially abundant in those portions of the myocardium. At their valvular attachment the fibrous bundles of the chordæ tendineæ turn almost at right angles, and spread out, in a somewhat radial manner, to become continuous with the dense fibrous tissue which forms the interior of the valve.

The *columnæ carneæ* are columelliform projections of the myocardium into the ventricular cavity. They consist of cardiac muscle fibres, which are disposed in their long axis, and are covered by reflections and reduplications of the endocardium. The irregular contour of the ventricular cavities appears to be entirely due to the projecting *columnæ carneæ*.

These muscular columns may present any one of three modes of attachment to the myocardium: (1) They may be attached along their entire extent; (2) they may be attached only at their two ends, the mid-portion being free; (3) they may be attached to the myocardium at one end only, the other end projecting into the ventricular cavity as a papillary muscle, from whose apex chordæ tendinæ pass to the auriculo-ventricular valves. Either of the last two forms may, in transections of the ventricles, appear as isolated islands of muscular tissue surrounded by endocardium and lying apparently free within the cavity of the ventricle.

Blood vessels.—The heart is supplied with blood through the coronary arteries. The larger branches of these vessels pursue their course beneath the epicardium in the superficial grooves of the cardiac wall. From these large arteries, smaller branches are distributed to the epicardium and to the muscular wall, the latter vessels penetrating as far as the endocardium, in whose connective tissue they form a meager capillary plexus.

The capillaries of the myocardium are extremely abundant. They form elongated meshes between the muscle fibres, the circumference of each muscle fibre being in relation with several capillary vessels. The veins return the blood from these rich capillary plexuses and pursue a course similar to that of the arteries, the larger veins being always found in the broader connective tissue septa.

NERVE SUPPLY.—The nerve supply of the vascular system is by means of fine branches derived from the cerebro-spinal and sympathetic systems. **In the heart** these minute nerve trunks end in the various cardiac ganglia, most of which are found in the connective tissue of the heart, e. g., the coronal plexuses about the orifices of the aorta and pulmonary artery. From these ganglia sensory nerve fibres are distributed to the endocardium and epicardium, and motor fibres to the myocardium. The most of the former are connected with the vagus, the latter with the sympathetic trunks.

From the cardiac ganglia branches pass to form a coarse plexus

in the connective tissue between the muscle bundles, the perimysial plexus, from the branches of which a fine plexus is distributed to the endomysium. The terminal branches end in relation with the surface of the muscle fibres.

The **blood vessels** are similarly supplied, minute ganglia occurring here and there in the adventitia or adjacent connective tissue. From these ganglia sensory branches are distributed to the adventitia and intima and motor branches to the tunica media. Naked nerve fibrils can be traced to the smallest blood vessels, and even in the capillaries terminal fibrillæ are found in relation with the endothelial wall.

CHAPTER VIII

THE NERVOUS TISSUES

THE nervous tissues include those tissue elements which are peculiar to the nervous system. The essential unit of structure, comparable to the cell of other tissues, is here the neurone. A *neurone* is a nerve cell in the broadest sense of the term. It consists of the *cell body* (nerve cell of the older writers, perikaryon), together with all of its processes. These latter are divisible into two varieties, the *neuraxone* and the *dendrites*.

The neurones are among the largest cells of the body. Their cell body is of variable size, in some cases extremely minute, at other times sufficiently large to be readily observed with the naked eye. Their processes, usually of considerable number, vary in length from a millimeter or less, up to half the height of man. It is therefore obviously impossible to study microscopically at one time the entire course of these longer processes. This circumstance renders it advisable to retain the term *nerve fibre* of the older writers to designate, not as was the former conception, a histological entity, but rather that portion of those long processes of the nerve cell which pursues its course, as a rule, outside of the grey matter of the central nervous system.

On this basis we may divide the neurone into the nerve cell and the nerve fibre. The former term includes the cell body with its dendrites and the proximal portion of its neuraxone, the distal portion of the neuraxone forming the essential part of a long nerve fibre. The nerve cells are found throughout the grey matter of the central nervous system and in the ganglia of the peripheral cerebro-spinal and sympathetic systems. Nerve fibres occur in the white matter of the central nervous system and in the nerve trunks and ganglia of the peripheral system.

In the peripheral nervous system the nervous tissues are chiefly supported by the connective tissues, but in the central nervous

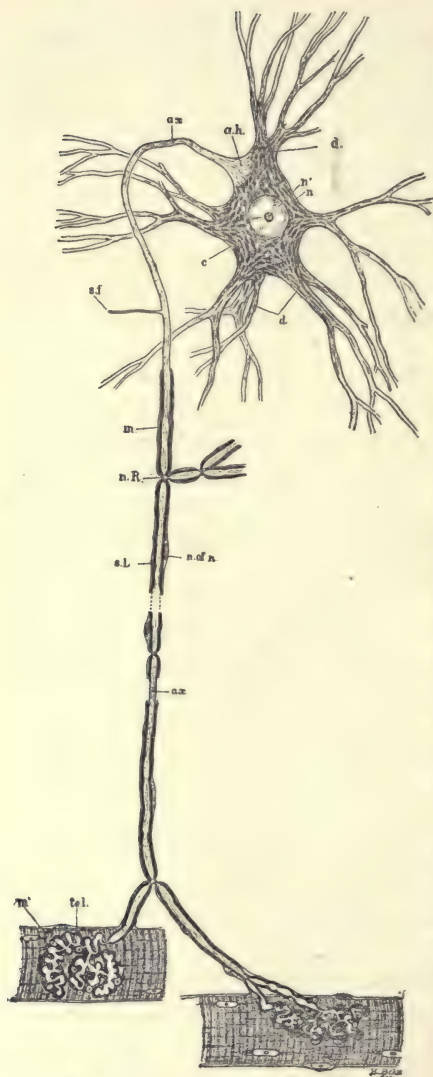


FIG. 100.—DIAGRAM OF A NEURONE.

a h, axone hillock; *a x*, neuraxis; *c*, cytoplasm, the Nissl granules have been stained; *d*, dendrites; *m*, myelin sheath of the nerve fibre; *m'*, muscle fibre; *n*, nucleus; *n'*, nucleolus; *n of n*, nucleus of the neurilemma of the nerve fibre; *n R*, node of Ranvier; *s f*, collateral; *s L*, segment of Lantermann; *tel*, telodendria or terminal arborization which here forms a motor end-plate. (After Barker.)

system a special form of supporting tissue, the neuroglia, is also found.*

THE NERVE CELL (*cell body, perikaryon, ganglion cell*).—This term, as already stated, includes the cell body with its dendrites and the proximal portion of its long neuraxis. The cell bodies vary in size from 4 to 200 μ in diameter. Their shape is chiefly dependent upon the number of their processes. Unipolar nerve cells, with but a single process, are flask-shaped or pyriform; bipolar cells, whose processes are usually derived from opposite extremities, are most frequently fusiform; multipolar nerve cells, from the considerable number of their processes, are irregularly stellate.

Nucleus.—The cytoplasm of the cell is finely granular, and contains a large vesicular nucleus which, as a rule, is eccentrically situated. The appearance of this large nucleus is quite characteristic of the nerve cell, as distinguished from the cells of

* See chapter xxiii.

other tissues. The nuclear membrane is distinct and highly chromatic. The contents of the nucleus, however, except for the large spherical nucleolus which is quite constantly present, is noticeably deficient in chromatin. Those few small karyosomes which are present are mostly adherent to the inner surface of the nuclear membrane. The achromatic nucleoplasm forms the greater portion of the nucleus. Occasionally the chromatin forms still finer granules, and is more equally distributed throughout the nucleus. A large, chromatic, centrally situated nucleolus is nearly always present.

Cytoplasm.—The finer structure of the cytoplasm of the nerve cell is the



FIG. 101.—A UNIPOLAR GANGLION CELL OF A FROG.

a, cell body; *b*, neuraxis; *c*, dendrite. Methylene blue. Highly magnified. (After von Sminnow.)



FIG. 102.—ISOLATED NERVE CELLS FROM THE SPINAL CORD OF MAN.

x, neuraxis. Carmin. $\times 160$. (After Sobotta.)

subject of considerable difference of opinion. The studies of Nissl have shown that it is divisible into a substance which is readily stained by methylene blue, thionin, etc. (the stainable substance of Nissl, tigroid of von Lenhossék), and an apparently homogeneous substance which is not so readily stained (the unstainable substance of Nissl).

Nissl's substance, or tigroid, occurs in the form of flake-like granules of varying size and irregular shape. Their disposition within the cytoplasm is subject to considerable variations in dif-



FIG. 103.—NERVE CELL FROM THE OLFACTORY BULB OF A RABBIT.
An arkyochrome nerve cell in the parapyknomorphous condition. Highly magnified. (After Nissl.)

ferent nerve cells. Yet it has been found that nerve cells occupying the same position in any given animal species always present the same type of structure as regards the disposition of their Nissl granules. According to Nissl, the following types may be distinguished:

A. **SOMATOCHROME NERVE CELLS**, in which the nucleus is surrounded by a considerable cytoplasmic body.

1. *Arkyochrome nerve cells*, whose stainable substance occurs in the form of an irregular network. These cells are widely distributed among the sensory nuclei of the spinal cord and medulla.

2. *Stichochrome nerve cells*, whose stainable substance presents a linear arrangement, the rows of granules being more or less nearly

parallel either to the nuclear membrane or to the surface of the cell. These cells are most abundant in the motor nuclei of the spinal cord and brain.

3. *Gryochrome nerve cells*, whose stainable granules present a tendency to agglutinate into clumps or threads. These cells are less numerous, but may be found in the corpus striatum.

4. *Arkyostichochrome nerve cells*, whose stainable granules, while presenting a delicate network, show at the same time a dis-

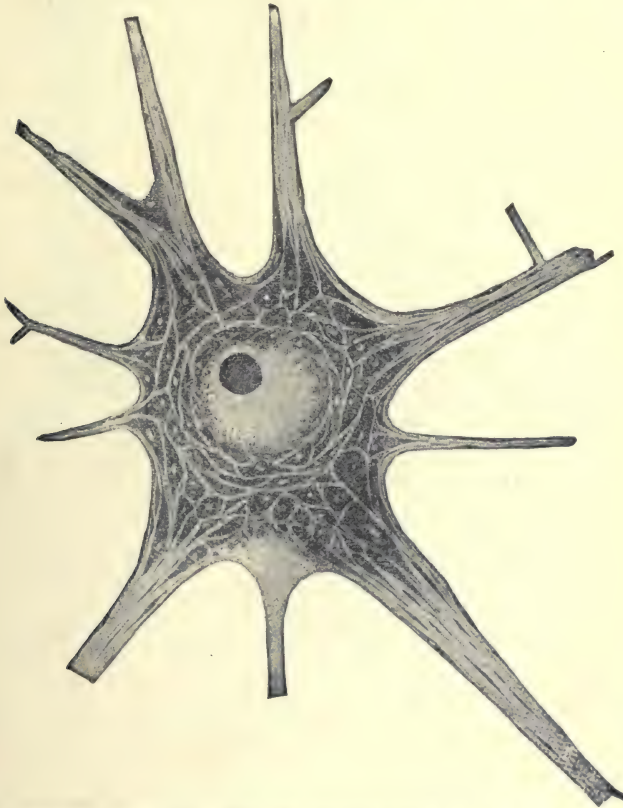


FIG. 104.—MOTOR NERVE CELL FROM THE VENTRAL HORN OF THE SPINAL CORD OF A RABBIT.

Of the three lower processes, the middle one represents the neuraxis. All the other processes are dendrites. The margins of the cell and of the masses of stainable substance appear too sharp in the reproduction. At the angle of division of the large dendrite at the left superior angle of the cell is shown one of the "wedges of division." This is classed as a stichochrome nerve cell in the apyknomorphous condition. Highly magnified. (After Nissl.)

tinctly linear arrangement. The Purkinje cells of the cerebellar cortex are offered as the only example of this type. Even these cells have lately been considered as belonging more distinctly to the arkyochrome variety (Nissl*).

B. CYTOCHROME NERVE CELLS, which present but very little cyto-

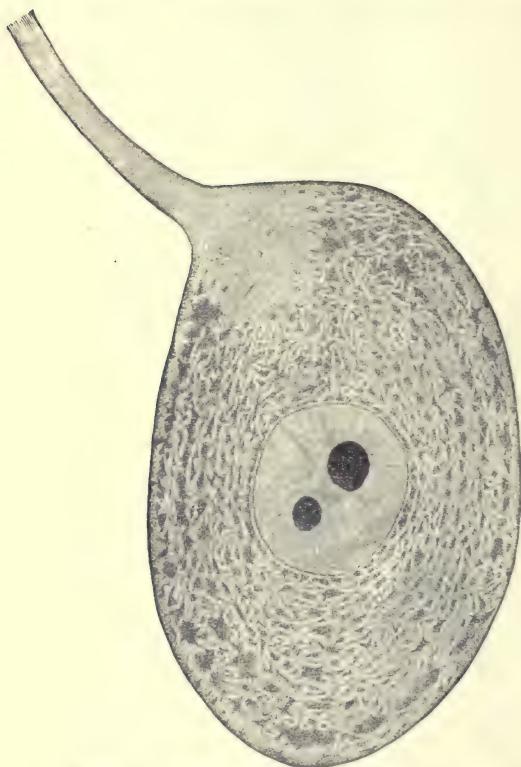


FIG. 105.—NERVE CELL FROM A GANGLION ON THE DORSAL ROOT OF A CERVICAL NERVE OF A RABBIT.

Stichochrome nerve cell in the apyknomorphous condition. Highly magnified. (After Nissl.)

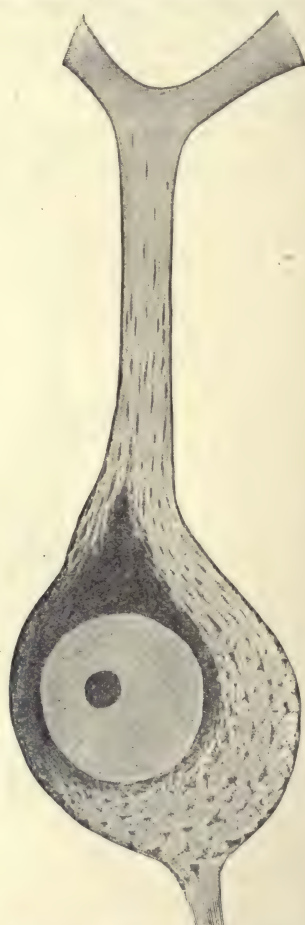


FIG. 106.—PURKINJE CELL FROM THE CEREBELLAR CORTEX OF THE RABBIT.

Arkyostichochrome nerve cell in the apyknomorphous condition. Highly magnified. (After Nissl.)

plasm, and whose nucleus is small, being only about the size of the ordinary leucocyte. Examples of this type are found in the granular layers of the cerebral and cerebellar cortex.

* Allg. Zeitschr. f. Psychiat., 1898.

C. KARYOCHROME NERVE CELLS, which also present but little cytoplasm, but whose nucleus is large, being equal in size to that of the average nerve cell. Such cells are also found in the granular layer of the cerebellar cortex.

Those nerve cells in which the Nissl substance is abundant are said to be in a *pyknomorphous*, those in which it is scanty in an *apyknomorphous* condition. The Nissl granules are apparently used up during functional activity of the nerve cell.

The majority of the coarse granules of stainable substance of Nissl present an irregular spindle shape; this is particularly true of those which show a linear arrangement. They are sometimes so grouped as to form two characteristic structures, the nuclear caps and the division wedges. *Nuclear caps*, as their name indicates, are accumulations of Nissl substance, which occur at the poles of the nucleus; one, two, or three of these caps may be in relation to a given nucleus. *Division wedges* occur in the dendrites, at the point of their division. The wedges are of a triangular shape, their concave base spanning the angle formed by the two subdivisions of the dendritic process.

Concerning the finer structure of the unstainable substance of Nissl comparatively little is known. With varying methods of fixation this portion of the cellular cytoplasm has been found to show very fine fibrils (Schultze, Flemming, Apáthy, Bethe) and fine acidophile granules (neurosomes of Held). Besides these structures there remains a homogeneous ground substance or hyaloplasm, which, though of extreme physiological importance, in the usual histological preparations presents no structure. Centrosomes and attraction spheres have been frequently observed in the nerve cells of the lower vertebrates, and occasionally in those of mammals.

The cytoplasm of many nerve cells contains a characteristic brownish-yellow *pigment*, whose fine granules have a tendency to

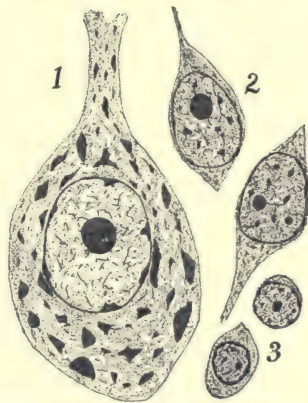


FIG. 107.—NERVE CELLS OF THE CEREbellAR CORTEX.

1, cell of Purkinje; arkyochrome type; 2, nerve cell of the granular layer; caryochrome type with a large nucleus; 3, a granule cell of the granular layer; cytochrome type with a small nucleus equal in size to that of a leucocyte. Nissl's stain. $\times 1200$.

accumulate in the vicinity of the nucleus. End fibrils of other nerve cells have been demonstrated within the cytoplasm of the nerve cell. Apáthy has likewise demonstrated that fibrils occasionally pass from one neurone to another, so that we no longer consider that a neurone, though a structural unit, is in all cases anatomically independent of all other neurones. The present status of this much discussed question seems to be comparable to that of the cell, as a histological unit of structure, which, though formerly thought to exist independently of other cell units, has since been found to be frequently connected, as by the intercellular bridges of epithelium and of smooth muscle, the syncytial tissues, etc. The neurones of the nervous system, therefore, while being usually related to one another by contiguity or by contact only,

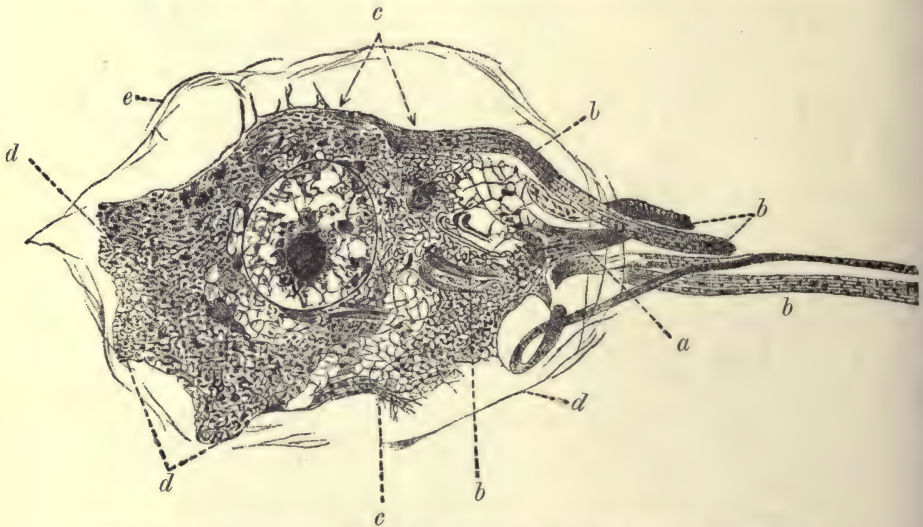


FIG. 108.—A NERVE CELL FROM THE TRAPEZOID NUCLEUS IN THE MIDBRAIN OF A RABBIT.

a, neuraxis; *b*, neuraxes of other nerve cells which terminate in relation and apparently fuse with the cytoplasm of the cell body; *c*, points of fusion or zones of conrescence; *d*, dendrites which have been cut off close to the cell body; *e*, neuroglia. Iron hematoxylin. Very highly magnified. (After Held.)

may occasionally be more directly connected by fibrillæ, which pass from the processes of one neurone to the cell body or processes of a second neurone (Apáthy, Bethe), or by "conrescence," as described by Held.

The nerve cells are surrounded by a narrow interval which

separates them from the surrounding tissue. This is presumably a lymphatic or tissue juice space. Holmgren has recently demonstrated, also, the presence, within the cytoplasm of the nerve cell, of minute canaliculi which form an intracellular network, more abundant near the surface of the cell, and which he has termed juice canaliculi (*Saftkanälchen*). These canaliculi may possibly account for the peculiar intracellular network which Golgi has recently demonstrated in the periphery of the nerve cell by a modification of his rapid silver impregnation method.

The processes of the nerve cell are of two varieties: the one, broad, granular, and rapidly dividing in the vicinity of the cell body into a number of branching subdivisions, is the dendrite; the other, long, slender, and finely fibrillar, arises from the cell body direct, or from the base of a dendrite, and, passing for a considerable distance from the cell body, finally enters the nerve fibre as its axis cylinder, or terminates in relation to some distant nerve cell. This latter process is the neuraxis. Each cell body usually possesses a single neuraxis and several dendrites. Cells without a neuraxis are found in the retina and in the olfactory bulb; except for these, all nerve cells in the body of man possess a neuraxis and usually but one such process. The subdivision of nerve cells into uni-, bi-, and multi-polar cells is, therefore, chiefly based upon the number of their dendrites.

Dendrites (*protoplasmic processes*).—The dendrites of a nerve cell vary from one to a considerable number. They arise from the cell body by a broad stem, and quickly break into branches which can be traced for a considerable distance—in fact, the arborization of the dendrites is usually so extensive that it can be followed for only a short portion of its course. Occasionally dendrites do not branch until they have arrived at a considerable distance from their parent cell body.

The structure of the dendrite is, to all appearances, similar to that of the cell body. The stainable substance of Nissl is continued for some distance into the arborizing dendrites, which often possess a finely fibrillar appearance. In Golgi-stained prepa-



FIG. 109.—INTRACELLULAR NETWORK WITHIN A PURKINJE CELL OF THE CEREBELLUM OF "STRIX FLAMMEA."

Golgi's stain. (After Golgi.)

rations the dendrites frequently present a thorny appearance, due to the clustering along their borders of minute lateral projections, the *gemmules*.

The terminal filaments of the dendritic arborization are frequently in relation with the cell bodies or neuraxes of other neurones, less frequently with the dendrites of other neurones.

The **neuraxis** (*neuraxon*, *dendron*, *neurite*, *axone*, *axis cylinder process*).—This process, in contradistinction to the dendrite, is long and slender, as a rule does not arborize near its parent cell body, is of smooth and regular contour in Golgi preparations, and contains no stainable substance of Nissl. It arises from the cell body, or less frequently from the base of a dendrite, by a conical, clear area, the axone hillock, which, like the process itself, is devoid of Nissl's stainable granules.

At some little distance from the parent cell body the neuraxis gives off very fine lateral branches, the *collaterals*, which leave the



FIG. 110.—GOLGI CELL, TYPE I, FROM THE SPINAL CORD OF A HUMAN FETUS.

At * is the relatively straight neuraxis which has already given off one collateral. Golgi's stain. (After von Lenhossék.)

parent stem at nearly right angles. These delicate branches finally terminate by a sudden *end arborization*, or end brush, by which each neuraxis is placed in relation with a large number of neurones.

The parent stem of the neuraxis may be finally exhausted in its collaterals, or it may in turn end in a terminal arborization. Collaterals are said to be more frequent in the proximal than in the distal portion of the neuraxis.

According to the length of their neuraxis, neurones were divided by Golgi into two types:

1. Golgi cells, Type I (Deiter's cells).
2. Golgi cells, Type II (Golgi's cells).

The cells of Type I possess a long neuraxis which passes beyond the confines of the grey matter in which it arises and usually becomes the axis cylinder of a nerve fibre.

The cells of Type II possess a short neuraxis which forms its terminal arborization in the vicinity of its parent cell body. The cells of this type are usually association neurones; they place in conduction relation other not very remote neurones. The cells of Type I, on the other hand, are more frequently projection neurones; they are distributed from the nerve centers to other and perhaps very different tissues, their course lying in the long projection tracts and nerve trunks of the nervous system.

The cells of Type II are therefore most frequently intrinsic or endogenous neurones, their whole course lying in one division of the central nervous system, e. g., the grey matter of the spinal cord. The cells of Type I are more frequently extrinsic or exogenous; they arise in one part of the nervous system to be distributed to a distant portion, e. g., they arise in the peripheral ganglia and enter the spinal cord to terminate in its grey matter, or *vice versa*.

THE NERVE FIBRE.—The origin of the nerve fibre and its relation to the other portions of the neurone will be appreciated by tracing the course of the neuraxis of a motor nerve cell of the ventral horn of grey matter in the spinal cord. This process, arising in the central grey matter, is at first a naked neuraxis. It soon leaves the grey matter to traverse the white matter and makes its exit from the spinal cord as the axis cylinder of one of the fibres of an anterior nerve root. On leaving the grey matter

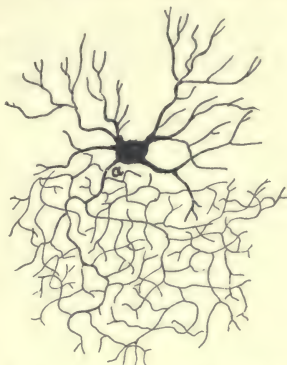


FIG. 111.—GOLGI CELL, TYPE II.

a, neuraxis, which immediately breaks into a network of fine collaterals. Golgi's stain. (After Andriezen, from Obersteiner.)

the neuraxis acquires a cylindrical sheath of myelin substance, the *medullary sheath*, *myelin sheath*, or *white substance of Schwann*.

On entering the anterior nerve root, which lies outside of the white matter of the spinal cord, the neuraxis receives a connective tissue sheath, the *neurilemma* or *nucleated sheath of Schwann*. The neuraxis retains these two sheaths until near its termination, when the sheaths suddenly stop, the neuraxis becoming again naked as it breaks into terminal fibrils.

Not all nerve fibres are medullated, nor do they all possess a nucleated sheath of Schwann. The neuraxes of the central nervous system are not supplied with a neurilemma until they pierce the meninges to enter the nerve roots. Those of the grey matter also have no appreciable medullary sheath. The neuraxes of the peripheral nerve trunks and ganglia are all supplied with a neurilemma except at their terminals, as already explained. Yet some of the peripheral neuraxes have a medullary sheath, while others have none. A neuraxis with its enveloping sheaths constitutes a nerve fibre, and upon the presence or absence of these sheaths nerve fibres may be classified as follows :

- | | |
|----------------------------------|----------------------------|
| A. Medullated nerve fibres..... | { 1. With a neurilemma. |
| | { 2. Without a neurilemma. |
| B. Non-medullated nerve fibres.. | { 3. With a neurilemma. |
| | { 4. Without a neurilemma. |

1. Medullated Nerve Fibres with a Neurilemma.—Nearly all the nerve fibres of the cerebro-spinal nerve trunks and ganglia and some of those of the sympathetic nerves are of this type. These nerve fibres consist essentially of three cylindrical structures : the *axis cylinder*, which is the continuation of the neuraxis of a nerve cell, and which forms the central portion or core of the nerve fibre ; the *medullary sheath*, which forms a hollow cylinder inclosing the axis cylinder, and which suffers frequent interruptions, as will be described ; and the *neurilemma*, which is an extremely thin investing sheath of connective tissue origin, and forms an uninterrupted envelope from the point where the nerve fibre leaves the central nervous system to a point near the end of the fibre where the axis cylinder breaks into its terminal fibrils. To these structures an investing sheath of connective tissue, the sheath of Henle, is sometimes added. It is derived from the connective tissue *endoneurium* in which the nerve fibres are embedded. It serves to support the capillary blood vessels destined for the supply of the nerve fibres.

The **axis cylinder** presents a finely fibrillar structure. The nature of these fibrils is not well understood. In certain nerve fibres of the lower animals these fibrils have a tendency to collect into the center of the axis cylinder, leaving a peripheral clear zone; this distribution is especially characteristic of those fibres which are not supplied with a medullary sheath. In mammals, however, the fibrillæ occupy a large portion of the axis cylinder, the clear peripheral area being correspondingly diminished until in man it can scarcely be recognized. The fibrils of the lower animals are also coarser.

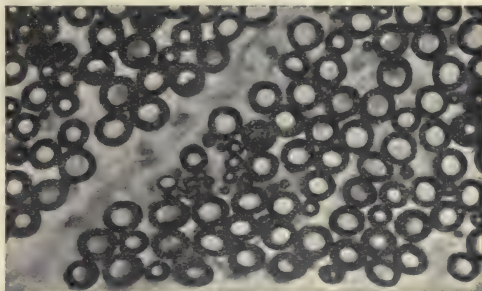


FIG. 112.—A SMALL PORTION OF A TRANSECTION OF THE SCIATIC NERVE OF A DOG.

Nerve fibres are seen in transection; their myelin sheaths are black, their neuraxes unstained. Osmium tetroxid. Photo. $\times 700$.

Apáthy, studying chiefly the lower animals, has considered these "*ultimate fibrillæ*" to be the conducting element of the nerve fibre. Others, however, lay greater stress upon the intervening clear portion, the *neuroplasm* of Schiefferdecker, as containing the active conducting element of the fibre.

The axis cylinder is, under certain conditions, at least, found to be inclosed by an extremely delicate membrane, the *axilemma* of Kühne. The existence of this membrane as an integral part of a living axis cylinder has been denied by others.

The **medullary sheath** (*white substance* of Schwann, *myelin sheath*) forms a cylindrical investment for the axis cylinder. It appears to be retained in position by the neurilemma, for when the latter is ruptured the myelin exudes in the form of "myelin drops." The *myelin* thus obtained possesses the physical properties of a fat. It is also capable of being blackened by osmium tetroxid. By extraction with ether the myelin can be removed, leaving behind a network of *neurokeratin*. It has not yet been proved that this network exists in the living nerve fibre.

At frequent intervals in the course of the nerve fibre its myelin sheath suffers complete interruption, thus forming the annular constrictions or *nodes of Ranvier*. At these points the neuro-

lemma dips in until it is in contact with the axis cylinder. Both axis cylinder and neurilemma are continued past the node without interruption.

The successive nodes of Ranvier divide the nerve fibre into *interannular segments*. Within each interannular segment the medullary sheath, on blackening with osmium tetroxid, presents clear intervals which penetrate the myelin sheath in such manner as to give the appearance of obliquely disposed clear lines or incisions. These *incisures of Schmidt* (*Schmidt-Lantermann lines*) have not been satisfactorily explained and can not be demonstrated in the living fibre, yet they present a constant form and are always present in osmic preparations.* These incisures subdivide the interannular segments of the medullary sheath into *medullary segments*.

In preparations of fresh nerve fibres which have been treated with silver nitrate according to the method of Ranvier, the solution is found to enter the fibre most readily at the nodes of Ranvier, so that if blackened by exposure to the sunlight, minute $+$ -like appearances are seen at each node. By prolonged maceration in weak solutions of silver nitrate

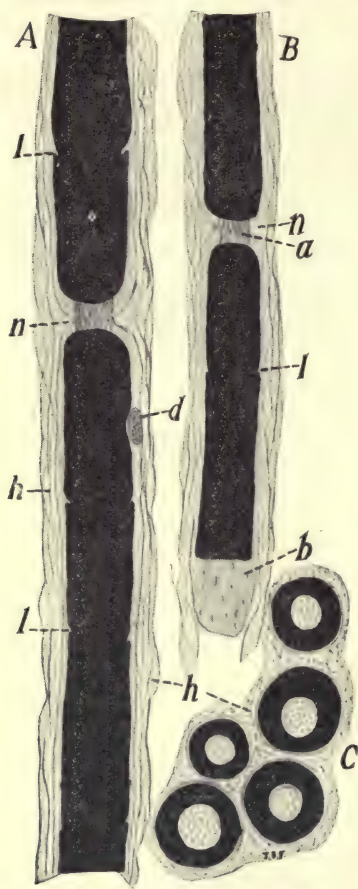


FIG. 113.—NERVE FIBRES.

A and B, from the sciatic nerve of a rabbit, isolated by teasing, and viewed in profile; C, a group of nerve fibres in trans-section, from the sciatic nerve of a dog. a, neuraxis; b, neurilemma projecting beyond the torn end of the fibre; d, nucleus; h, endoneurium or fibrous sheath of Henle; l, Schmidt-Lantermann lines; n, nodes of Ranvier. Osmium tetroxid. A and B, $\times 670$; C, $\times 900$.

* Schmidt originally considered them to be the optical expression of folds in the outer fibrous coats. Lantermann and others have shown that they are within the neurilemma.

the solution penetrates still farther and the blackened axis cylinder is found to possess spiral transverse markings which are quite characteristic. The true meaning of these appearances has not been satisfactorily explained.* Because of the apparent greater permeability of the fibre at these points, these peculiarities have been taken to indicate a certain relation of the annular constrictions to the nutrition of the fibre.

The neurilemma (*nucleated sheath of Schwann*) is the outermost of the nerve fibre sheaths. It is of distinctly mesoblastic origin and makes its appearance prior to the medullary sheath. It forms a very delicate membrane, which incloses the myelin substance, and at each node of Ranvier comes into contact with the axis cylinder.

Attached to the inner surface of the neurilemma in each internode, and usually but one for each internodal segment, is an oval nucleus. The nucleus is surrounded by a minute amount of finely granular cytoplasm. This structure is taken to indicate that the embryonal neurilemma is formed by connective tissue cells which become spread out over the surface of the primitive fibre, one cell, as a rule, supplying each internodal segment, and its nucleus with a minute amount of undifferentiated protoplasm is, according to this hypothesis, considered to remain as a permanent part of the neurilemma.

2. Medullated Nerve Fibres without a Neurilemma.—This type of nerve fibre composes the white matter of the central nervous system. The axis cylinder does not, of course, differ in the least from those of the previous variety and will need no further description.

The medullary sheath is, also, similar in its finer structure to that of the previous type, but since no neurilemma is present, these fibres possess no nodes of Ranvier. The medullary sheath of the fibres found in the white matter of the brain and spinal cord is, therefore, uninterrupted. Its surface is in direct contact with the neuroglia network, which forms the supporting tissue of these organs.

3. Non-medullated Nerve Fibres with a Neurilemma (*sympathetic nerve fibres, Remak's fibres*).—The most of the fibres of the sympathetic system are of this type. The axis cylinder does not differ from that of the previous types. The medullary sheath is

* They have been usually considered to be artifacts.

either entirely absent or, at most, very insignificant in these fibres. The neurilemma is perhaps incomplete at times, but exhibits frequent nuclei along the course of the fibre. Fibres of this type are of quite frequent occurrence in the cranial nerves of the cerebro-spinal system. Other cerebro-spinal nerve fibres lose their medullary sheath and finally also their neurilemma prior to their termination.

4. Non-medullated Nerve Fibres without a Neurilemma.—These fibres are naked axis cylinders and as such are found at the cytoproximal end of the neuraxis in the grey matter of the central nervous system, and at the cytodistal end prior to the termination of the neuraxis in its arborization of terminal fibrils. In man nerve fibres are of this type throughout their entire course, only in the olfactory nerves.

NERVE TRUNKS.—The nerve fibres of the peripheral nervous system are united into bundles to form the *nerve trunks* or *nerves*.

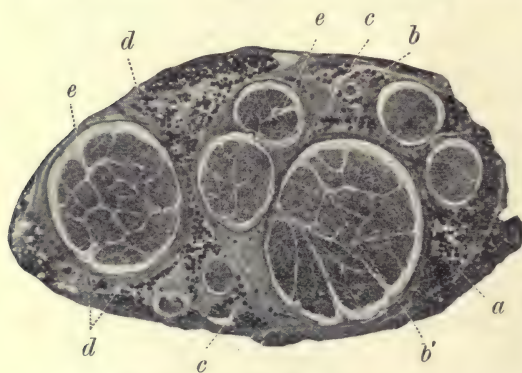


FIG. 114.—TRANSECTION OF THE SCIATIC NERVE OF A DOG.

The fat cells and the myelin sheaths of the nerve fibres have been blackened by osmium tetroxid. *a*, fat cells; *b*, *b'*, blood vessels, that at *b'* lies within a funiculus; *c*, epineurium; *d*, perineurium; *e*, coarser bands of the endoneurium. Osmium tetroxid. Photo. $\times 30$.

Each nerve is surrounded by a heavy connective tissue sheath, the *epineurium*, which sends trabeculum-like septa into the nerve. These septa subdivide the nerve trunk into smaller bundles of nerve fibres, the *funiculi*. The funiculus forms a compact bundle of nerve fibres, and is in turn invested with a sheath of dense connective tissue,

the *perineurium*. Hence the perineurium stands in the same relation to the funiculus as does the epineurium to the whole nerve trunk.

From the inner surface of the perineurium, septa pass into the funiculus and break up to form a fine connective tissue framework between the individual nerve fibres. Thus the nerve fibres are embedded in a delicate connective tissue sheath. On teasing the

nerve fibres with needles this fibrous endoneurium remains adherent to the surface of the nerve fibre and gives the appearance of an outermost fibrous sheath, the so-called connective tissue *sheath of Henle*.

Nerve trunks frequently branch, the branches being formed either by an individual funiculus or by groups of funiculi. In the smaller nerve trunks the funiculi are further subdivided. It is by anastomosis of the funiculi that most of the nerve plexuses are formed. Individual nerve fibres of the medullated type do not branch except in those portions which are naked axis cylinders, viz., at the cytoproximal portion of the neuraxis by means of collaterals, and at the cytodistal portion by means of end arborizations. Occasionally also the nerve fibre divides at a node of Ranvier.

Vascular Supply.—The nerve trunks are well supplied with *blood vessels*. The larger of these are found in the epineurium, and from them branches of considerable size enter the septa to be distributed through the perineurium to the funiculi. The coarser septa of the endoneurium contain minute arteries and veins. A capillary network with elongated meshes occupies the finer divisions of the endoneurium, its vessels being thus brought into contact with the nerve fibres.

Perivascular *lymphatic vessels* abound in the epineurium and its septa, and lymphatic tissue spaces are found throughout the connective tissue of the nerve trunk. Where the cerebro-spinal nerve trunks penetrate the meninges these lymphatic vessels are said to be continuous with the similar vessels of the dura mater.

Minute nerve fibre bundles, *nervi nervorum*, are also found in the epineurium; their fibres are mostly, if not entirely, distributed to the blood vessels.

GANGLIA.—A ganglion may be described as a group of nerve cells occurring in the course of a peripheral nerve trunk. The largest of the ganglia form fusiform swellings in the course of the nerve, which are visible to the naked eye. The smallest, on the other hand, contain not more than half a dozen nerve cells, and these must be sought with the aid of the microscope and can only be found by the most careful observation.

Whatever may be their size, all ganglia appear to have a similar structure, except for those differences which characterize the sympathetic as distinguished from the cerebro-spinal type. The

essential elements of structure are the nerve cells, nerve fibres, and a supporting framework of rather dense connective tissue.

Many of the nerve cells of the adult mammal are unipolar in the cerebro-spinal ganglia, but are usually multipolar in the sympathetic. The spinal ganglia of the lower vertebrates and of the embryo mammal, however, contain bipolar ganglion cells. In mam-

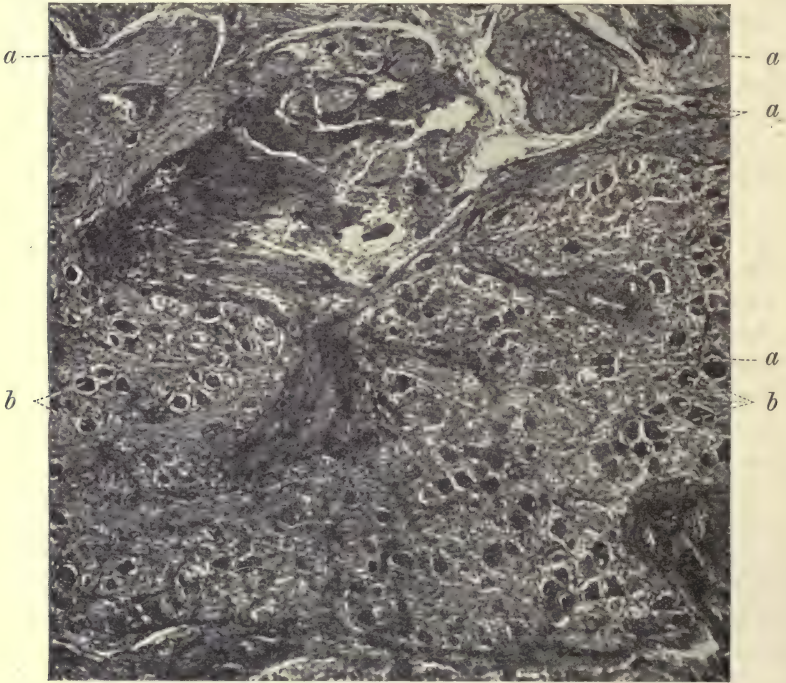


FIG. 115.—A SMALL PORTION OF A HUMAN GASSERIAN GANGLION.

a, funiculi derived from the nerve trunk; *b*, nerve cells. Hematein and eosin. Photo. $\times 60$.

mals the two processes fuse to form a single one which branches in a Y- or T-like manner soon after leaving the parent cell body.

The nerve cells of all ganglia are surrounded by a peculiar connective tissue capsule. It is composed of flattened endotheloid connective tissue cells which form a complete investment for the nerve cell and are continued on to its processes, possibly becoming continuous with the neurilemma. The capsule is not, as a rule, closely applied to the cell, but leaves a narrow interval which is occupied by lymph or "tissue juice."

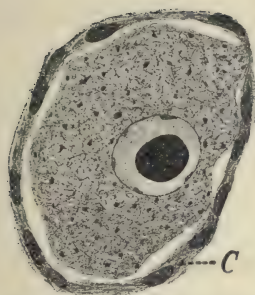


FIG. 116.—A NERVE CELL FROM A SECTION OF A HUMAN GASSERIAN GANGLION.

C, capsule. Nissl's stain. $\times 500$.

other, especially in the sympathetic system, where they were formerly but little understood. In the *spinal ganglia* Dogiel* describes two types of ganglion cells: (1) in which the processes are thick and pass out of the ganglion to become the axis-cylinder of a medullated nerve fibre, and (2) cells with slender processes which break up within the ganglion and whose terminal branches form a pericapsular plexus around the cell capsule; from this plexus fine end branches penetrate the capsule to form a pericellular arborization about the nerve cell itself. The cells of this latter type might be said to serve as

In its finer structure the ganglionic neurones do not appear to differ in any way from other neurones. The large vesicular nucleus with its distinct nucleolus readily distinguishes these cells from those of neighboring tissues.

Recent studies of the ganglion cells by Dogiel, Ranvier, and Cajal have done much to explain the relations of these cells to each

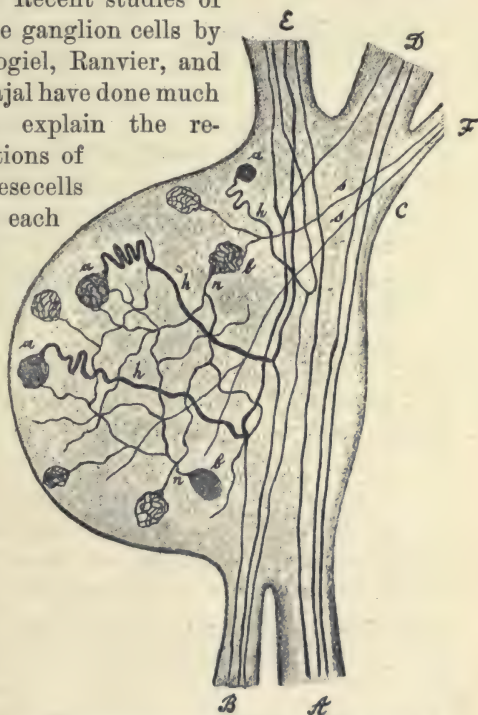


FIG. 117.—SCHEMATIC REPRESENTATION OF THE RELATIONS OF THE STRUCTURES COMPOSING A SPINAL GANGLION.

A and B, ventral and dorsal spinal nerve roots; C, a spinal nerve; D and E, its ventral and dorsal divisions; F, its ramus communicans. *a*, nerve cells of the *first type*, whose neuraxes divide and form the axis cylinder of a peripheral and a central nerve fibre; *b*, nerve cells of the *second type*, whose neuraxes, *n*, end in a felt work about the cells of the first type; *s*, sympathetic nerve fibres which terminate in a basket work about the cell bodies of the second type of ganglion cells. (After Dogiel.)

* Anat. Anz., 1896.

association neurones within the ganglion. Nerve fibres from the sympathetic ganglia also enter the spinal ganglia and form pericellular arborizations about the cells of the second type. Dogiel also finds that multipolar ganglion cells occur in the spinal ganglia of the adult as well as of the embryo.

In the *sympathetic ganglia* Dogiel* likewise recognizes two cell types: (1) small multipolar fusiform or stellate nerve cells with 5 to 20 dendrites and a neuraxis which enters the nerve trunks as a non-medullated fibre, but may later acquire a thin medullary sheath; (2) larger spheroidal nerve cells with 1 to 16 dendrites and a single neuraxis which also enters the nerve trunk as a non-medullated nerve fibre, but may later acquire a very thin medullary sheath. The dendrites of Type II are distinguished from those of Type I by being very long and slender and also by entering the nerve trunks, to pass, presumably, to neighboring ganglia. The dendrites of the first cell type, on the other hand, are shorter, thicker, and end in relation with other cells within the same ganglion.

The ganglionic cell group is eccentrically placed as regards the axis of the nerve trunk, some funiculi apparently passing the ganglion without being in any way connected with its nerve cells.

The sympathetic differ from the cerebro-spinal ganglia chiefly in the preponderance of non-medullated nerve fibres in the former and of the medullated type in the latter. Just as the cerebro-spinal ganglia receive a few non-medullated sympathetic fibres, so also the sympathetic ganglia receive, through the medium of the rami communicantes, a certain number of medullated nerve fibres from the cerebro-spinal system. Moreover, with the intense staining method of Weigert very thin medullary sheaths may now be demonstrated where formerly they were not suspected.

The ganglia are supplied with blood vessels and lymphatic vessels in a manner similar to the nerve trunks in whose course they occur.

*Anat. Anz., 1896.

CHAPTER IX

PERIPHERAL NERVE TERMINATIONS: END ORGANS

ALL peripheral nerve fibres end either as terminal fibrils or in relation to a highly specialized end organ. The function of these latter bodies is apparently included in the changing of ordinary stimuli—mechanical, thermal, chemical, etc.—into a nerve impulse, or, *vice versa*, the changing of a nerve impulse to a cell stimulus which results in motion, secretion, etc., according to the nature of the tissue cells which are thus stimulated. Some of the nerve end organs are connected with centrifugal (motor) fibres, others with centripetal (sensory) fibres. Nerve endings are found in nearly all the tissues of the body with the exception of cartilage and the calcareous tissue of the bones.

NERVE ENDINGS IN EPITHELIUM

Intra-epithelial nerve fibrils are derived from nerve fibre plexuses in the subjacent connective tissue; the epithelium usually receives a very abundant nerve supply. The following types of intra-epithelial nerve endings have to be considered.

I. END FIBRILS.—This form of nerve termination has been demonstrated in all the varieties of epithelium. Terminal nerve fibres enter the epithelial tissue as naked fibrils, often somewhat varicose, which form a



FIG. 118.—NERVE ENDINGS IN THE EPITHELIUM OF THE LARYNX.

On the left a taste bud; on the right, nerve endings in the stratified epithelium are represented. (After Retzius.)

delicate plexus between the epithelial cells. The terminal fibrils of this plexus frequently end in minute knob-like enlargements

which are in contact with the surface, but rarely, if ever, penetrate the interior of the epithelial cells. The "*trefoil plates*" of Bethe represent unusually large end knobs.

II. **TACTILE CELLS** (Merkel).—These are modified epithelial cells, with clear cytoplasm and a slightly vesicular nucleus, which



FIG. 119.—TACTILE CELLS IN THE EPITHELIUM OF THE GROIN OF A GUINEA-PIG.

a, tactile cell; e, epithelial cell; m, tactile meniscus, at the end of a nerve fibril; n, nerve fibre. Chlorid of gold. Highly magnified. (After Ranvier.)

are found in the deeper layers of the stratified epithelium of the epidermis and in the root sheaths of hairs. These cells are recognized by their vesicular character and by the fact that they occur most abundantly in the inter-papillary portions of the epidermis. The deeper surface of the tactile cell rests in a cup-like expansion of a terminal nerve fibril which is known as the *tactile meniscus*.

III. **NEURO-EPITHELIUM**.—The cells of some types of neuro-epithelium, e. g., the olfactory cells, are true nerve cells; others are modified epithelial cells, in relation to which the nerves terminate by intercellular end fibrils. The neuro-epithelium of the eye and the ear will be described in the chapters devoted to these organs, that of the gustatory organ forms typical nerve end organs, the taste buds.

IV. **TASTE BUDS** (*gustatory organ*).—These end organs appear to be concerned with the special sense of taste. They occur in the stratified epithelium of the base of the tongue, uvula, soft palate, and epiglottis. Disse has also found similar structures in the nasal mucous membrane. They are most abundant on the lateral surfaces of the circumvallate papillæ of the tongue and on the walls of the sulci in the foliate papillæ which are most highly developed in the rabbit. They are occasionally found on the fungiform papillæ of the tongue, where they occur in considerable numbers in fetal life but mostly disappear before birth, and in the lateral walls of the sulci about the circumvallate papillæ.

Taste buds are ovoid, ellipsoidal, or spheroidal masses which occupy almost the entire depth of the epithelial layer. Their

broad base rests upon the basement membrane, their narrower apex extends nearly to the surface of the epithelium. The apex of the bud is thus covered by the superficial squamous epithelial cells except for a narrow tubular opening which overlies the superficial pole of the end organ. This canal presents an external and an internal ostium, respectively designated the outer and inner *taste pore*. The inner taste pore leads into a goblet-shaped depression in the apex of the taste bud, into which the cuticular processes of the gustatory cells project (von Ebner *).

The taste buds consist essentially of two varieties of cells, the gustatory and the sustentacular. The latter include the broad outer sustentacular or tegmental cells at the surface of the bud, the inner sustentacular cells within, and the basal cells which lie near the basement membrane.

The **gustatory cells** are slender neuro-epithe-

lial structures whose nucleus causes a fusiform enlargement near their center or toward the basal end. Their cytoplasm is finely granular; their nucleus stains deeply and is ovoid or rod-shaped. The distal end of the cell carries a delicate, highly refractive cuticular process which projects beyond the apices of the sustentacular cells and as far as the inner taste pore. Their proximal end is often bifid, forked, or so flattened as to form a foot-like extremity which is connected with the basal cells by fine processes.

The outer and inner **sustentacular cells** are elongated epithelioid cells, having an ovoid or spheroidal vesicular nucleus which causes no bulging of the protoplasm, and a coarsely reticular and frequently vacuolated cytoplasm. The distal ends of the cells

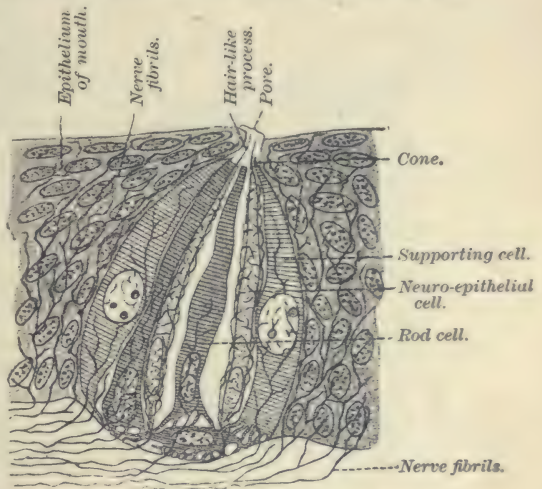


FIG. 120.—SCHEMATIC REPRESENTATION OF A TASTE BUD.

(After Hermann, from Böhm and von Davidoff.)

taper to blunt points, which collectively form the lateral wall of v. Ebner's goblet-shaped cavity at the apex of the taste bud. The proximal end is broad, often blunt or serrated, and, like the gustatory cells, it is connected with the basal cells by protoplasmic processes.

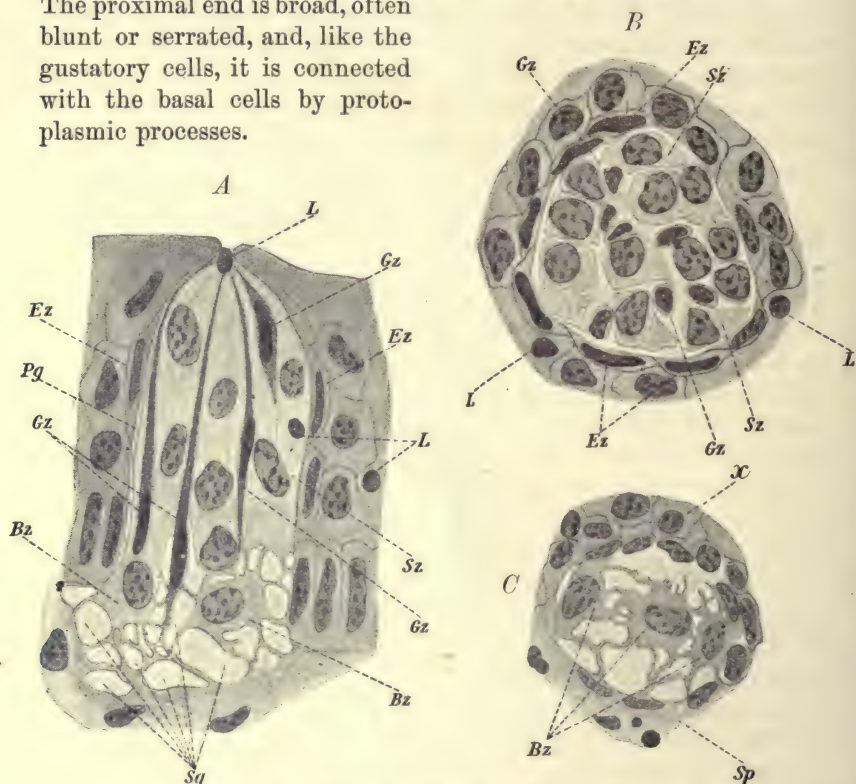


FIG. 121.—TASTE BUD FROM THE HUMAN TONGUE.

A, in longitudinal section; *B*, transection through the deeper third; *C*, transection through the base. *Bz*, basal cells; *Ez*, extra-bulbar cells; *Gz*, gustatory cell; *L*, leucocytes, in *A* one of these is seen in the pore; *Pg*, perigemmal space; *Sg*, Subgemmal spaces; *Sp*, connective tissue of the tunica propria; *Sz*, sustentacular cells; *x*, cells of the adjacent epithelium. (After Graberg.)

The **basal cells** (Hermann) are flattened bodies with small ovoid vesicular nuclei and a relatively small amount of cytoplasm which is prolonged into numerous processes that appear to be continuous with the sustentacular and gustatory cells. These cells have been considered as having a similar function to the sustentacular cells.

The nerve fibrils of the taste buds are derived from a sub-epithelial plexus which distributes terminal fibrils to the gustatory

and sustentacular cells—*intragemmal fibres*—and to the intervening portions of the stratified epithelium—*intergemmal fibres*—where they terminate in end fibrils. Von Lenhossek * states that the intragemmal and intergemmal fibres are never derived from the same nerve fibre. *Circumgemmal* fibres, distributed as varicose fibrils to the surface of the taste bud, may, however, arise from the same nerve fibre as the intragemmal branches.

Those nerve fibres which enter the taste buds form fine varicose fibrils which are closely applied to, but are not continuous with, the gustatory and the sustentacular cells. The terminal twigs of these fibrils end by minute end knobs which are scarcely distinguishable from the varicosities (Fig. 118).

NERVE ENDINGS IN CONNECTIVE TISSUE

The nerve fibres form extensive plexuses in the connective tissues from which terminal branches are distributed to the epithelium, the walls of the blood and lymphatic vessels, and to the numerous sensory end organs which occur in great abundance in most of the connective tissues. Nerves also terminate in connective tissue by free end fibrils some of which, as in the epithelial tissues, possess minute end knobs. Free nerve endings of this nature occur in the tendons, the lungs, the stomachial and intestinal mucous membranes, the meninges, and in the superficial layer of the corium of the skin and the hair follicles (*terminaisons hédériformes* of Ranvier).

The following types of nerve end organs are found in connective tissue :

I. TACTILE CORPUSCLES (*touch corpuscles of Meissner*).—These organs are formed by the terminal expansion of a nerve fibre, which forms a varicose plexus inclosed within a delicate connective tissue sheath. The nerve fibre, or its primary branches, prior to its ultimate division makes several spiral turns about the corpuscle. The course

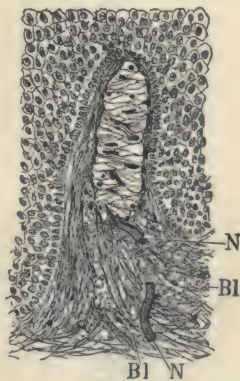


FIG. 122.—TACTILE CORPUSCLE OF MEISSNER FROM THE SKIN OF THE HUMAN TOE.

Bl, blood vessel; N, medullated nerve fibre. Highly magnified. (After Schiefferdecker.)

of the nerve fibre gives the corpuscle a peculiar spirally striated appearance. Within the corpuscle the nerve fibre breaks into a plexus of varicose fibrils, many of which end in knobbed extremities. The corpuscles also contain many flattened or cuneiform epithelioid cells which are interspersed among the nerve fibrils.



FIG. 123.—TACTILE CORPUSCLE OF MEISSNER.

a, nerve fibrils which enter the corpuscle and supply its nerve sheath. Methylene blue. Very highly magnified. (After Dogiel.)

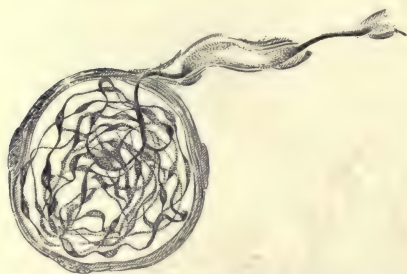


FIG. 125.—END BULB OF KRAUSE FROM THE MARGIN OF THE OCULAR CONJUNCTIVA.

The neuraxis forms a dense skein within the encapsulated bulb. Methylene blue. Highly magnified. (After Dogiel.)

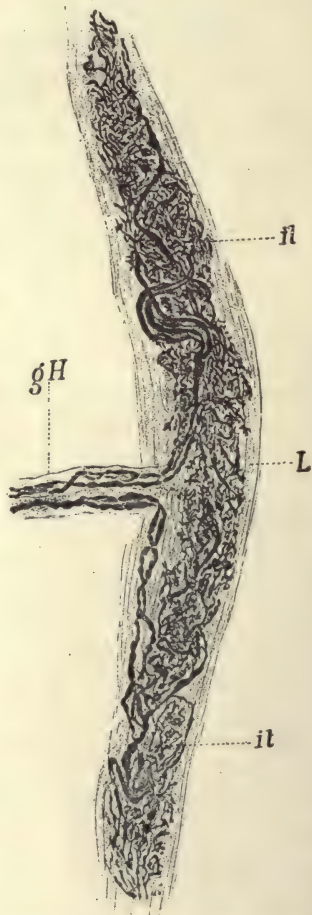


FIG. 124.—RUFFINI'S END ORGAN.

A single nerve fibre breaks up to form the tangle of nerve fibrils within the organ. *gH*, medullary sheath; *il*, terminal fibrils of the axis cylinder; *L*, connective tissue capsule. (After Ruffini.)

Tactile corpuscles occur in large numbers in the cutaneous *papillæ* of the finger tips and less abundantly in other portions of the skin; they have also been found in the conjunctiva

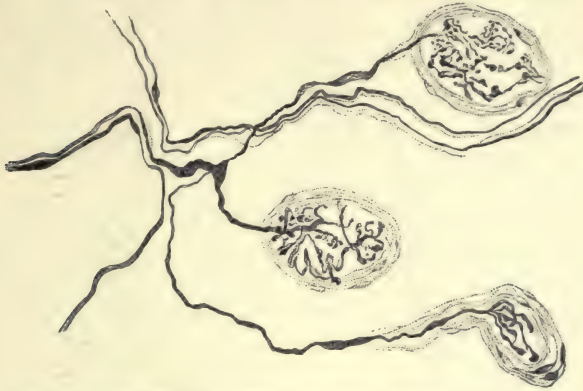


FIG. 126.—GENITAL CORPUSCLES FROM THE CLITORIS OF A RABBIT.

A single neuraxis from the nerve plexus enters each corpuscle. Methylene blue. Highly magnified. (After Retzius.)

(Dogiel *). They appear to be concerned with the finer tactile sensations.

II. RUFFINI'S END ORGANS.—These bodies resemble the tactile corpuscles in structure but possess a definite, though thin, connective tissue sheath within which the terminal arborization

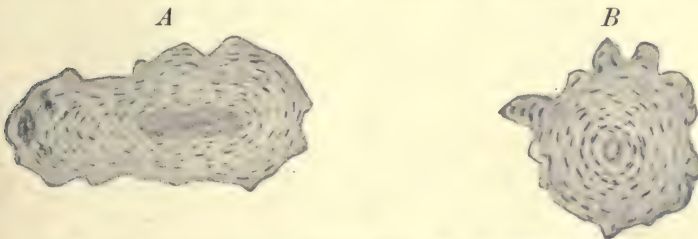


FIG. 127.—A PACINIAN CORPUSCLE FROM THE MESENTERY OF A CAT.

A, a nearly axial section; B, a transection. Hematein and orange G. $\times 410$.

of the nerve fibre is embedded in a granular core. They occur in the deeper part of the true skin near its junction with the subcutaneous tissue and in the connective tissue septa of the latter, whereas the tactile corpuscles are found in the papillary layer of

* Arch. f. mik. Anat., 1891.

the skin. Ruffini* states that they occur in large numbers in the skin of the finger tips. where they rival in number the rather more deeply placed Pacinian corpuscles.

The Ruffini organs are cylindrical in shape and their nerve fibres usually enter at the side of the organ, though occasionally at its end. Now and then a single branching nerve fibre is distributed to several of these end organs.

III. END BULBS (Krause).—These structures, together with those which follow, form the so-called *encapsulated nerve end organs*. In the end bulbs the nerve forms a terminal arborization of varicose and knobbed fibrils which freely anastomose (Dogiel, Ruffini). The bulb is invested with a distinct connective tissue capsule. On entering the bulb the nerve fibre loses its sheaths and the perineurium becomes continuous with the capsule of the bulb. Within the capsule the nerve

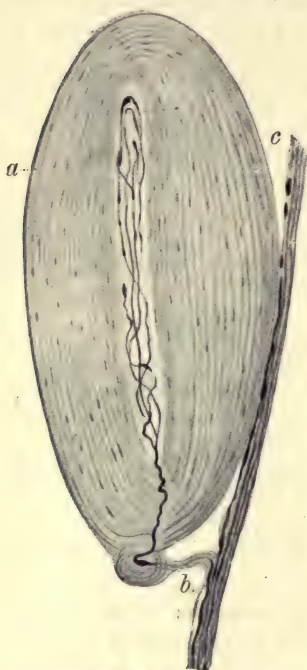


FIG. 128.—A PACINIAN CORPUSCLE FROM THE PLEURA OF A CHILD.

a, lamellæ; b, nerve fibre; c, nerve. Methylen blue. Moderately magnified. (After Dogiel.)

fibrils are embedded in a granular *inner bulb*.

The end bulbs vary much in both size and shape. They may be either spheroidal, ovoid, twisted or convoluted, branched or compound, or cylindroid. They are abundantly found in the conjunctiva, but also occur in the corium of the skin. Similar, though more highly developed, end bulbs form the so-called *genital corpuscles* which are found in considerable numbers in the connective tissue of the glans



FIG. 129.—PACINIAN CORPUSCLE FROM THE MESENTERY OF A KITTEN.

The nerve fibre shows lateral processes, many of which are knobbed. Methylen blue. Moderately magnified. (After Sala.)

* Arch. ital. de biol., 1894.

penis, prepuce, and clitoris. In some of the smaller end bulbs found in the tendons, the mucous membranes, and in certain portions of the skin, the nerve fibre fails to divide but ends near the distal extremity of the bulb in a small fusiform end knob.

IV. PACINIAN CORPUSCLES (*Vater's corpuscles*, *Vater-Pacinian corpuscles*, *lamellar corpuscles*).—These are among the largest of the nerve end organs. They assume the form of a large ovoid thickening, placed upon the end of a nerve fibre. The Pacinian corpuscle consists of a thick lamellated connective tissue



FIG. 130.—A PACINIAN CORPUSCLE IN LONGITUDINAL SECTION, SHOWING A NETWORK OF SPIRAL ELASTIC FIBRES.

Weigert's elastic tissue stain. Highly magnified. (After Sala.)

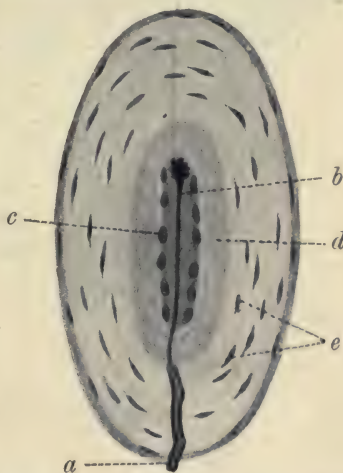


FIG. 131.—AXIAL SECTION OF A CORPUSCLE OF HERBST FROM A DUCK'S TONGUE.

a, medullated nerve fibre; *b*, naked axial nerve fibre with a bulbous end; *c*, nuclei of the core; *d*, inner concentric capsule; *e*, nuclei of the outer lamellated capsule. $\times 380$. (After Sobotta.)

coat, and a central granular protoplasmic core which is pierced by the nerve fibre. The medullated nerve fibre enters the axis of the corpuscle, its perineurium becoming continuous with the superficial capsule of connective tissue. The nerve fibre on entering the core loses its medullary sheath, and after traversing a greater or less portion of the core divides into two to five branches which end near the distal pole in a disk-like expansion.

In its course through the core, the nerve fibre gives off fine lateral twigs (Sala, Retzius).

The connective tissue sheath consists of a granular protoplasm which is permeated by densely felted spiral fibres (Sala) and is divided into ten to fifty concentric lamellæ by lines of flattened connective tissue cells and fibres. According to Schwalbe, however, these cells form an endothelial coat on either surface of each lamella. Pacinian corpuscles are occasionally compound, two or more adjacent corpuscles being supplied by branches of the same nerve fibre.



FIG. 132.—A PAPILLA OF THE DUCK'S TONGUE, CONTAINING A CORPUSCLE OF GRANDRY.

The corpuscle contains four large cells, between which are the tactile menisci of the nerve ending. *n*, nerve. Highly magnified. (After Merkel, from K  lliker.)

and in the connective tissue of the thyroid gland and of the skeletal muscles.

The **corpuscles of Herbst** (*Key-Retzius corpuscles*) are similar in structure to the Pacinian corpuscles except that the core which surrounds the axial nerve fibre contains cuboidal *tactile cells*. They occur only in the cere of aquatic birds.

The **corpuscles of Grandry** (*Merkel's corpuscles*), also found only in aquatic birds, contain several tactile cells of ectoblastic origin similar to those found in the epidermis. Each cell is in relation with a ring or meniscus formed by the expanded end of a nerve fibre. The whole is included within a thin connective tissue capsule and may be regarded as a *compound tactile cell* occurring in connective tissue.

The **Golgi-Mazzoni corpuscles**, described by Ruffini,* somewhat resemble the Pacinian corpuscles in that they possess a lamellar, though relatively very thin, connective tissue sheath and a cen-



FIG. 133.—GOLGI-MAZZONI CORPUSCLES FROM THE SUBCUTANEOUS TISSUE OF THE TIP OF THE FINGER. (After Ruffini.)

tral granular core. The core, however, is relatively excessive in size, and the entering nerve fibre breaks into a number of branches with discoid terminal expansions similar to those found in the nerve endings of Golgi in the tendons.

* Arch. ital. de biol., 1894.

NERVE ENDINGS IN MUSCLE AND TENDON

A. Striated Muscle

I. MOTOR END PLATES.—These organs form the intramuscular endings of peripheral motor neurones whose cell bodies are found in the ventral horns of the grey matter of the spinal cord. They reach the muscle through the many cerebro-spinal nerve trunks. On entering the muscle these nerves form a plexus in

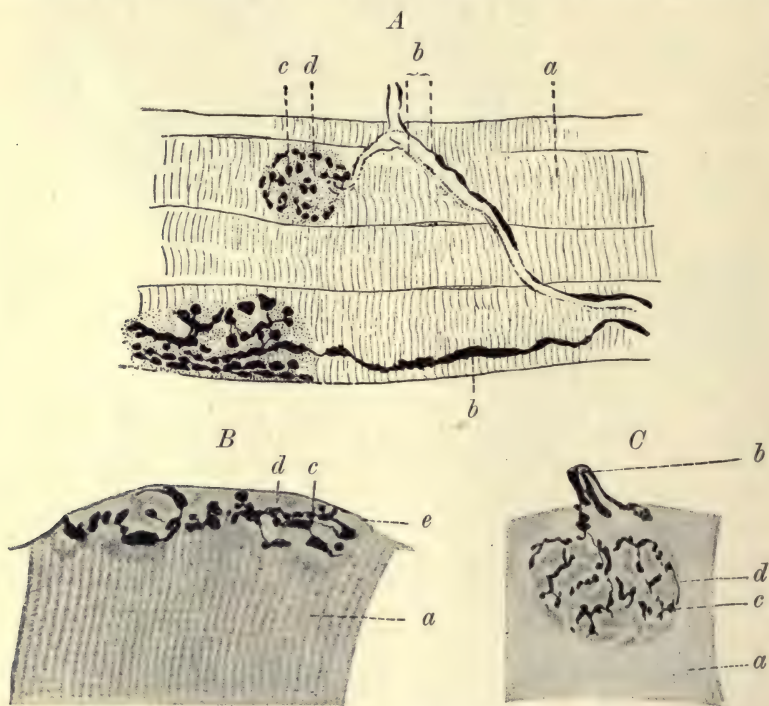


FIG. 134.—MOTOR NERVE ENDINGS IN STRIATED MUSCLE.

A, from a lizard; *B*, from the guinea-pig; *C*, from the hedgehog. *A* and *C* are surface views; in *B* the end plate is seen in profile. *a*, muscle fibre; *b*, nerve fibre; *c*, nerve ending in the form of a "brush"; *d*, the sole plate; *e*, sarcolemma. *A*, $\times 160$; *B*, $\times 700$; *C*, $\times 1200$. (After Böhm and von Davidoff.)

the perimysium from which nerve fibres are distributed within the muscle bundles. Here they form an abundant plexus of branching nerve fibres within the endomysium, the ultimate branches being of sufficient number to supply one or more terminal nerve fibres to each muscle cell.

At the surface of the muscle cell the nerve fibre loses its medullary sheath, its neurilemma becomes continuous with the sarcolemma of the muscle cell, and its naked axis cylinder divides into two to five branches, which end, often after repeated subdivision, in flattened terminal disks, distributed in mammals over a limited, in amphibians over a broad area, but which never completely encircle the cylindrical muscle cell.

The terminal expansions of the neuraxis rest upon a granular *sole plate* which contains many ovoid nuclei, the *sole nuclei*. The nature of these nuclei is somewhat uncertain. By those who consider, as is now generally accepted, that the nerve endings lie within the sarcolemma of the muscle fibre, the nuclei are presumed to be derived from the muscle cell and the granular substance of the sole plate is regarded as a modified portion of the sarcoplasm. Some authors (Kölliker, Krause) regard the end plates as lying *on* the muscle cell rather than within the sarcolemma, but the studies of Huber and De Witt,* as also those of many other observers, would seem to have satisfactorily settled this question in favor of the intramuscular interpretation. In this connection it is interesting to observe that motor end plates were discovered by Doyère in those muscle cells of insects which are not provided with a sarcolemma. In these cells, as in the muscles of many vertebrates, the entrance of the nerve produces a distinct eminence on the surface of the muscle fibre which is known as the eminence, elevation, or *hillock of Doyère*.

II. MUSCLE SPINDLES
(*Neuro-muscular spindles, neuro-muscular end organs*).—These are sensory nerve endings which are concerned with the so-called muscle sense and are found in nearly all the skeletal muscles.

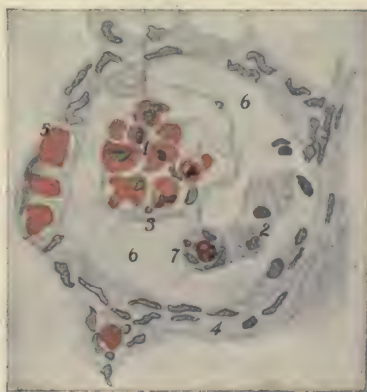


FIG. 135.—A MUSCLE SPINDLE FROM THE PSOAS MAGNUS OF MAN.

1, intrafusal muscle fibres; 2, nerve fibres; 3, axial sheath; 4, connective tissue capsule; 5, muscle fibres of an adjacent fasciculus; 6, peri-axial lymphatic spaces; 7, blood vessel. Hematein and eosin. $\times 470$.

* J. of Comparat. Neurol., 1898.

They are especially numerous in the extrinsic muscles of the tongue, in the small muscles of the hand and foot, and in the intercostal muscles (Huber *).

A muscle spindle contains from five to twenty striated muscle fibres of small size, and an almost equal number of nerve fibres. The whole is inclosed within a connective tissue capsule of considerable thickness. The bundle of *intrafusal muscle fibres* is again surrounded by a delicate *axial sheath* of connective tissue which is united to the capsule by bands of fine fibrous tissue

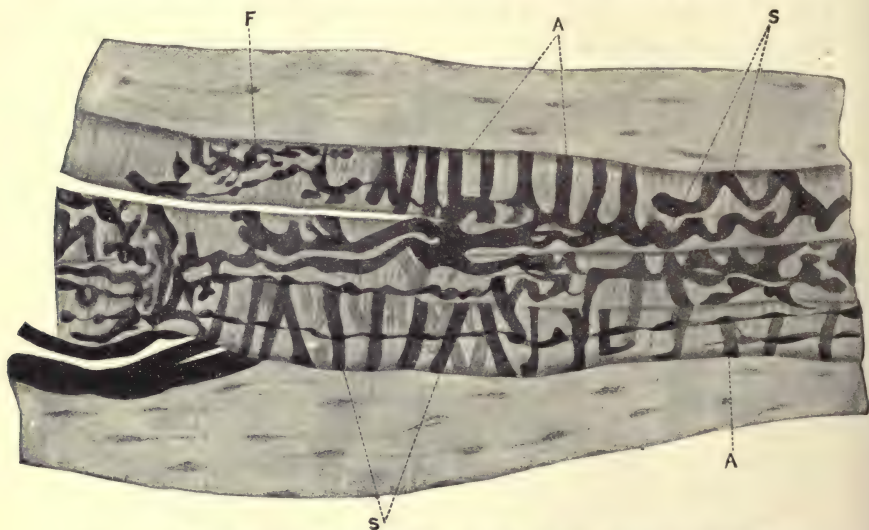


FIG. 136.—MIDDLE THIRD OF A TERMINAL PLAQUE IN THE MUSCLE SPINDLE OF AN ADULT CAT.

A, rings; F, dendritic branchings; S, spirals. Chloride of gold preparation. Highly magnified. (After Ruffini.)

which span the broad *periaxial lymphatic space*. The larger of these fibrous bands support the nerve fibres, on their way to the intrafusal muscle cells, together with several small blood vessels.

The muscle spindles form long fusiform bodies whose muscle fibres at the pole of the spindle may be connected with the tendon, or they may join other muscle fibre bundles. The muscle spindles are usually found in the fibrous septa of the perimysium.

* Am. J. of Anat., 1902.

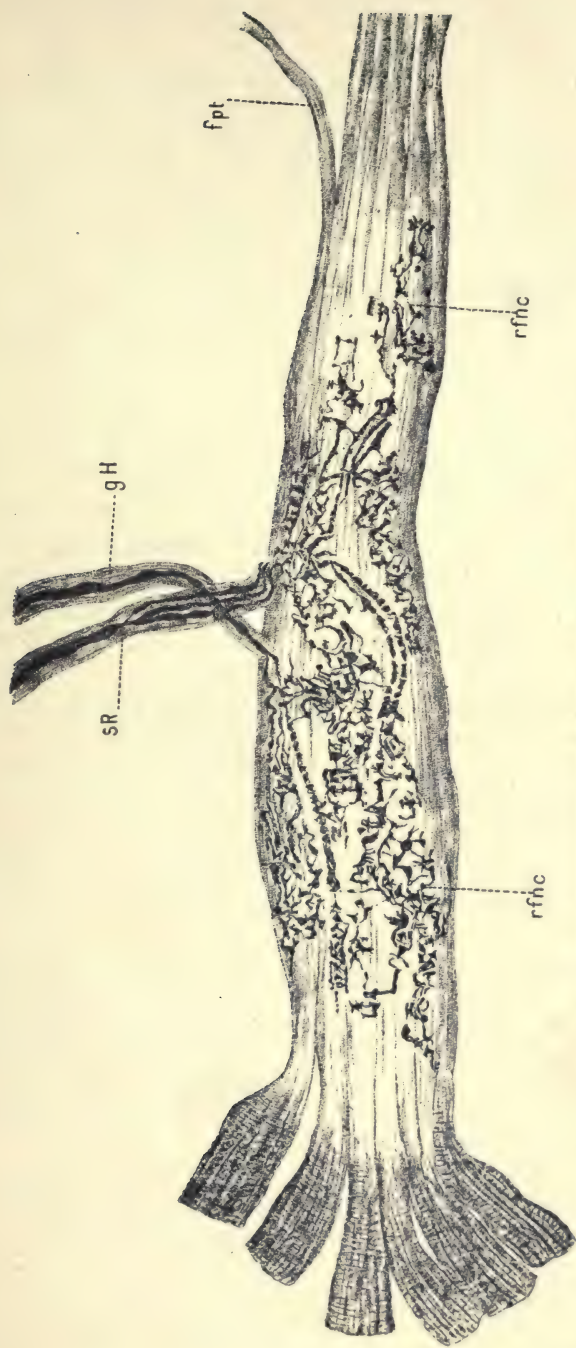


FIG. 137.—NEURO-TENDINOUS END ORGAN OR TENDON SPINDLE OF GOLGI.

fpt, bundle of tendon fibres; *gH*, medullated nerve fibre; *rfhc*, ribbon-like terminal ramifications of the neuraxis; *SR*, node of Ranvier. Moderately magnified. (After Ciacio.)

Either one or several nerve trunks enter the spindle, usually near its equator rather than at its poles. The nerve fibres branch repeatedly in the intracapsular connective tissue, and finally pierce the axial sheath as naked processes which form a rich arborization of terminal fibrils about the intrafusal muscle fibres. Ruffini distinguishes three types of terminal nerve fibrils: (1) *annular*, which form rings around the muscle fibres; (2) *spiral*, which are spirally twisted about the intrafusal fibres; and (3) *dendritic branchings* (*terminaisons à fleurs*), in which the neuraxes break into numerous irregular processes with laminate expansions.

Motor end plates for the muscle fibres of the spindle as well as sympathetic vaso-motor nerves for its blood vessels have also been demonstrated within the muscle spindles.

That the muscle spindles are sensory and not motor organs has been demonstrated by Sherington,* who found that they were not affected by the muscular atrophy following section of the peripheral motor neurones, and by Horsley † and others who have found that the muscle spindles are unaffected in cases of extreme muscular atrophy in man.

III. NEUROTENDINOUS END ORGANS (*Golgi end organs, tendon spindles*).—These organs occur in the tendons of muscles near the junction of the tendon bundles with the muscle fibres. They are fusiform in shape and consist of a thin lamellar capsule of connective tissue which incloses several intrafusal tendon bundles of dense fibrous tissue. A narrow lymphatic space intervenes between the capsule and the intrafusal tendon bundles.

Nerve fibres enter the spindle and give off several medullated branches which run between the tendon bundles near the axis of the spindle. These finally form naked end fibrils with branching end plates, which surround the tendon bundles in an annular or spiral manner (Ciaccio ‡). Since the structure of the Golgi tendon spindles closely resembles that of the muscle spindles, they are undoubtedly of similar function.

IV. In addition to the special motor and sensory end organs described above, **Pacinian corpuscles** and **end bulbs** of Krause are also found in the connective tissue of striated muscles.

* J. Physiol., 1894.

† Brain, 1897.

‡ Arch. ital. de biol., 1891.

B. Cardiac and Smooth Muscle

The nerves of the **heart** are distributed to the cardiac ganglia, whence non-medullated fibres pass to all portions of the organ and form a very rich plexus in the intermuscular connective tissue. Fine terminal fibrils are distributed from this plexus to the muscle fibres, upon whose surface they end in varicose swellings and end knobs. While most of these fibrils are probably motor in function, others which end in the intermuscular connective tissue are more probably centripetal.

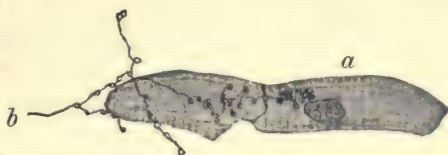


FIG. 138.—NERVE ENDINGS IN CARDIAC MUSCLE, FROM THE HEART OF A CAT.

a, muscle cells; *b*, nerve fibre. Methylen blue. Highly magnified. (After Huber and De Witt.)

In **smooth muscle** plexuses of sympathetic nerve fibres occur in the intervals between the bundles of muscle fibres. Secondary plexuses of naked fibrils are found among the muscle cells, and from this plexus fine lateral fibrils are distributed to the

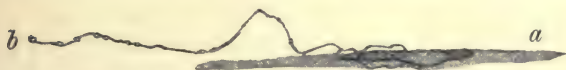


FIG. 139.—NERVE ENDINGS IN SMOOTH MUSCLE, FROM THE INTESTINE OF A CAT.

a, muscle cell; *b*, nerve fibre. Methylen blue. Highly magnified. (After Huber and De Witt.)

muscle cells, upon whose surface they end in small terminal granules or end knobs. Many of the nerve fibres in smooth muscle are undoubtedly of sensory function.

The nerve endings and the distribution of the peripheral nerve fibres in the various organs of the body are more fully described in the several chapters devoted to those organs.

CHAPTER X

THE LYMPHATIC SYSTEM

THE lymphatic series includes a system of lymphatic channels which collect the lymph from the various tissues of the body and return it to the large veins of the neck, where it mixes with the blood. In the course of this lymph vascular system are various aggregations of lymphoid or adenoid tissue which occur in the form of lymphoid nodules or follicles, lymphatic glands or nodes, and the lymphoid organs. These organs are the tonsils, thymus, and spleen. The lymphatic vessels also stand in intimate relation if not in direct communication with the serous and synovial membranes and the bursæ.

LYMPH.—Like the blood, the lymph may be considered as a primary tissue whose intercellular elements are entirely of a fluid nature. In most portions of the body, lymph is a colorless fluid which is scantily provided with corpuscular elements, the *lymphatic corpuscles*. The lymphatic corpuscles are identical with the leucocytes of the blood. In the lymph most of these cells are of the mononuclear form, the small mononuclears or lymphocytes being the most abundant. Lymph also contains a small proportion of polynuclear cells, which not only are derived from the lymphoid tissues, but as wandering cells find their way into the lymphatic vessels from the tissues generally.

In addition to the leucocytes lymph contains fat globules and glycogen. These are mostly the products of absorption from the intestinal tract, in which process the lymphatic vessels play an important rôle. In the lymphatic vessels of the intestine during absorption fat globules are so abundant as to impart to the lymph a milky white color; this variety of lymph is termed the *chyle*. These fat globules are rapidly removed by the lymphoid organs, since even in the presence of abundant chyle only comparatively few fat globules escape into the general blood current. The lymph of other portions of the body than the abdominal region, therefore, contains relatively little fat.

The lymph, unlike the blood, circulates in but one direction, viz., toward the heart. It must therefore be formed in the tissues generally. The blood plasma constantly escapes through the walls of the capillary vessels into the surrounding lymphatic spaces of the tissues. It is these tissue spaces which have been considered as forming the beginning of the lymphatic system. Recent evidence, however, goes to show that the tissue spaces are not directly connected with the lymphatic vessels, but that just as the plasma exudes into the tissue spaces by processes of secretion, osmosis, and filtration, so the *tissue juices*, as the predecessors of lymph, enter the lymphatic vessels by similar processes of secretion, osmosis, and filtration. Lymph is also formed by absorption, which occurs chiefly in the alimentary tract.

Under similar conditions the lymph as well as the blood will coagulate, the fibrin forming a firm, colorless clot in which the leucocytes are entangled. Because of their tendency to adhere to the sides of the vessel—thus circulating at the periphery of the current—the lymphatic corpuscles are most likely to be found at the periphery in those post-mortem clots which occur within the lymphatic vessels.

LYMPHATIC VESSELS (*lymphatics*).—The lymphatic vessels vary in size from that of the smallest capillary vessels up to that of the thoracic duct. The smaller vessels, lymphatic capillaries, form anastomosing meshes in all tissues where blood capillaries are found. They are most abundant in the perivascular connective tissues, where they form a dense plexus about the wall of the blood vessels.

The wall of the **lymphatic capillary**, like that of the blood capillary, consists of a single layer of endothelium. This endothelium probably forms a complete lining for the lymphatic capillary and is continuous through larger and larger vessels with that of the veins, from which, according to Sabin,* the lymphatics are originally developed.

The relation of the lymphatic capillaries to the tissue spaces is not as yet definitely settled. It was formerly thought that these spaces were continuous with the lymphatic capillaries, but the more recent observations, represented by those of MacCallum,† seem to show that the capillaries of the lymphatic system, like

* Amer. J. Anat., 1902.

† Johns Hop. Hosp. Bull., 1903; and Arch. f. Anat., 1902.

those of the blood vascular system, form a series of branching channels which are open only toward the veins. According to this conception, therefore, the tissue juices, formerly also considered as lymph, are contained within a separate series of channels, the tissue spaces and lymphatic canaliculi, and they enter the true



Fig. 140.—SUBCUTANEOUS LYMPHATIC VESSEL OF A FETAL PIG.

At the right is a small blood vessel. Hematein and eosin. Highly magnified. (After MacCallum.)

lymphatics only by processes of osmosis and the secretory activity of the lymphatic endothelia.

The lymphatic capillaries are of rather irregular caliber and possess frequent sinus-like dilatations, which peculiarity is also characteristic of the larger lymphatic vessels.

The lymphatic capillaries soon acquire an adventitial sheath of fibro-elastic tissue and pass into the smaller **lymphatic vessels**. On attaining a size of from 0.2 to 0.8 mm. their wall is differen-

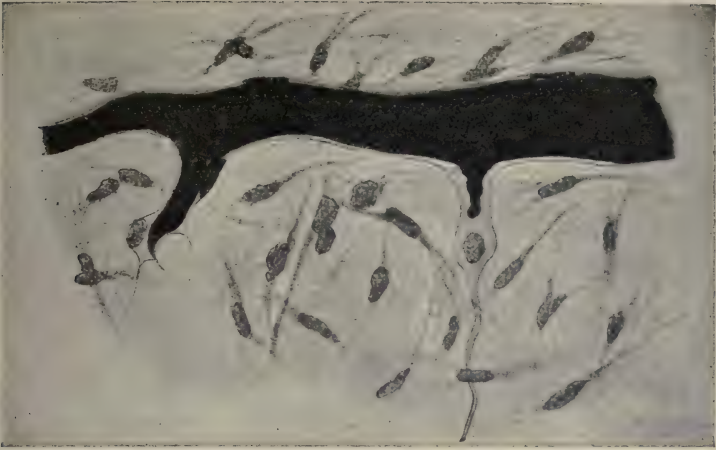


FIG. 141.—THE GROWING END OF A DEVELOPING LYMPHATIC VESSEL IN THE SUBCUTANEOUS TISSUE OF A FETAL PIG.

The lumen of the vessel has been filled with a dark injection mass. Highly magnified. (After MacCallum.)

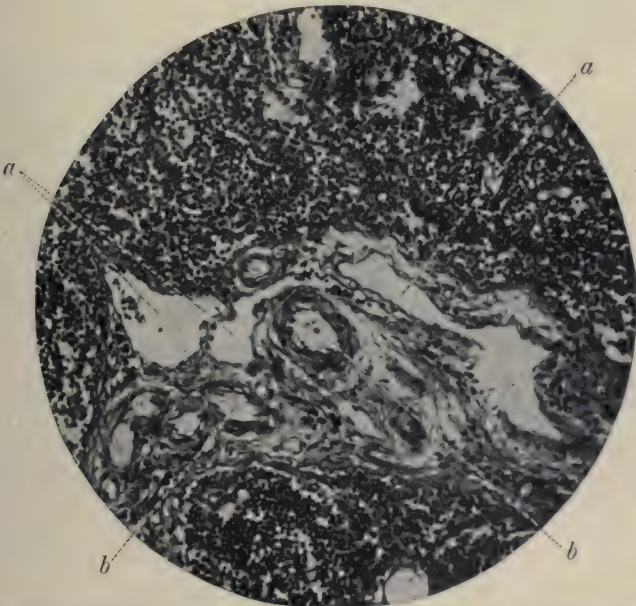


FIG. 142.—LYMPHATIC AND BLOOD VESSELS IN THE HILUM OF A HUMAN LYMPHATIC NODE.

a, lymphatic vessels; *b*, blood vessels. Hematein and eosin. *Photo. $\times 160$.

tiated into the same three coats which are found in the veins. Except for the fact that they contain lymph instead of blood, these vessels closely resemble the small veins, and like the latter vessels they possess frequent valves.

The tunica intima of the lymphatic vessel consists of an endothelial lining with a thin delicate fibro-elastic membrane. The

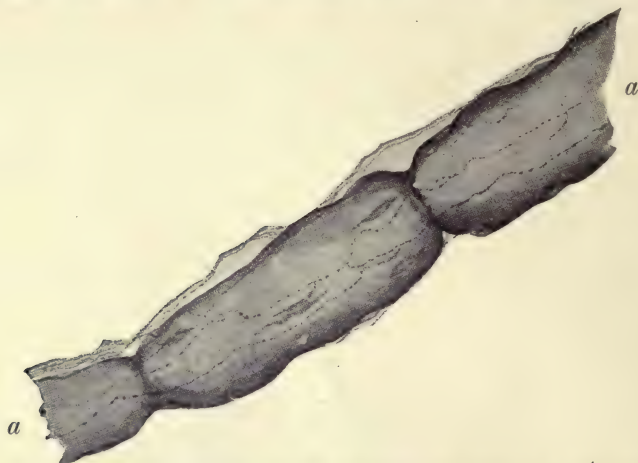


FIG. 143.—LYMPHATIC CAPILLARY FROM THE SPERMATIC CORD OF A DOG, SHOWING NERVE ENDINGS.

a, nerve fibres. Methylen blue. Highly magnified. (After Kytmanof.)

tunica media is thin and contains circular smooth muscle fibres. The adventitia is the thickest coat of the lymphatic vessel. It consists of fibrous connective tissue and longitudinally disposed bundles of smooth muscle fibres.

The wall of the lymphatic vessels is supplied with small blood-vessels and nerves, in the same manner as the veins. The nerves form a plexus in the adventitia from which branches are distributed to the media and intima. Kytmanof* has traced the fine nerve fibrils to the smallest lymphatic capillaries, where, as in the intima of the larger vessels, they end in close relation to the endothelial cells.

To summarize: the lymphatic capillaries arise by one of three methods:

1. As lymphatic plexuses in all connective tissue; the most abundant of these are the perivascular lymphatics.

* Anat. Anz., 1901.

2. As dilated pouches having blind extremities, as in the villi of the small intestine.

3. By direct communication with the stomata of the serous membranes.

The lymph is derived from the tissue juices and by absorption from the alimentary tract, and is conveyed by the lymphatic capillaries to larger and larger lymphatic vessels, which resemble the small veins in their structure, and which finally empty into the subclavian veins of the neck.

THE SEROUS MEMBRANES.—The serous membranes form closed sacs which line the great cavities of the body and are reflected over the viscera to form a double covering, the two layers of which are freely movable over one another. Of these two layers the one, the parietal layer, is attached to the wall of the body cavity, the other, the visceral layer, covers the surface of the inclosed organ.

The serous membranes consist of an *endothelial lining* and a supporting membrane of areolar connective tissue which is richly supplied with capillary blood vessels and lymphatics. The endothelium consists of large flat cells, pavement epithelium, whose serrated margins are firmly united by an intercellular cement substance. Here and there minute openings are seen which are surrounded by very small endothelial cells; these *stomata* have been found to be in certain instances directly connected with the lymphatic vessels.

Tunica Propria.—The endothelium rests upon a layer of areolar tissue which is richly supplied with small blood vessels and lymphatics, forming an abundant vascular plexus beneath the endothelium. The serous membrane is either directly united to the wall of the cavity and the surface of the organ which it envelops, or it may be attached by a looser layer of “*subendothelial connective tissue.*”

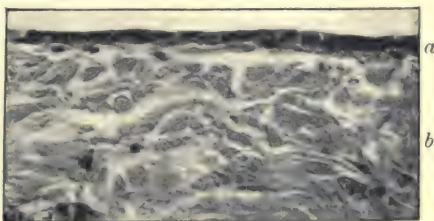


FIG. 144.—TRANSECTION OF THE PERICARDIUM OF A CHILD.

a-a, endothelium; *b-b*, subendothelial connective tissue. Hematein and eosin. Photo. $\times 500$.

The thickness of the endothelial cells varies in different portions of the serous membranes and is somewhat dependent upon

the age of the individual. In most portions it is no more than a pavement epithelium, but over the surface of the functionally active ovary these cells are much thickened and acquire a cuboidal



FIG. 145.—SECTION OF A VASCULAR SYNOVIAL VILLUS FROM THE KNEE JOINT OF A CHILD.

Hematein and eosin. Photo. $\times 200$.

shape; thus it forms the “germinal epithelium” of the ovary. In young individuals, viz., in fetal life and early childhood, the cuboidal cell type is found in many portions of the peritoneum, pleura, and pericardium.

The **synovial membranes** resemble the serous in their structure. They are lined by a single layer of pavement cells which is said to

be incomplete in places. Its endothelium is supported upon a layer of firm fibrous tissue richly supplied with both lymphatic and blood capillaries. In the recesses of the joints the synovial membranes are frequently thrown into small villous folds, which are chiefly formed by the inner portion of the fibrous coat and are covered with endothelium; these are the synovial villi.

The **bursæ** and the synovial sheaths of the tendons are of similar structure.

Both the serous and the synovial membranes are moistened by fluid which contains leucocytes in small numbers, and closely resembles the lymph and tissue juice in its composition.

LYMPHATIC FOLLICLES (*Lymphatic Nodules*).—The lymphatic follicle is a structural unit of lymphoid tissue which may exist independently, as in the solitary follicles of the intestinal tract, or may form groups or accumulations consisting of a greater or less number of follicular units. In this latter condition they occur in the mucous membrane of the small intestine as

Peyer's patches, in the tongue as the lingual tonsil, in the fauces as the faucial tonsils, in the pharynx as the pharyngeal tonsil, in the wall of the laryngeal cavity, in the spleen as the Malpighian corpuscles, in the lymphatic glands as the peripheral lymphatic follicles, and in the thymus, where we may consider the lobule of the organ as being the structural equivalent of a lymphatic follicle.

The lymphatic follicle consists of a mass of lymphoid tissue, usually of ovoid form, which is surrounded by or embedded in

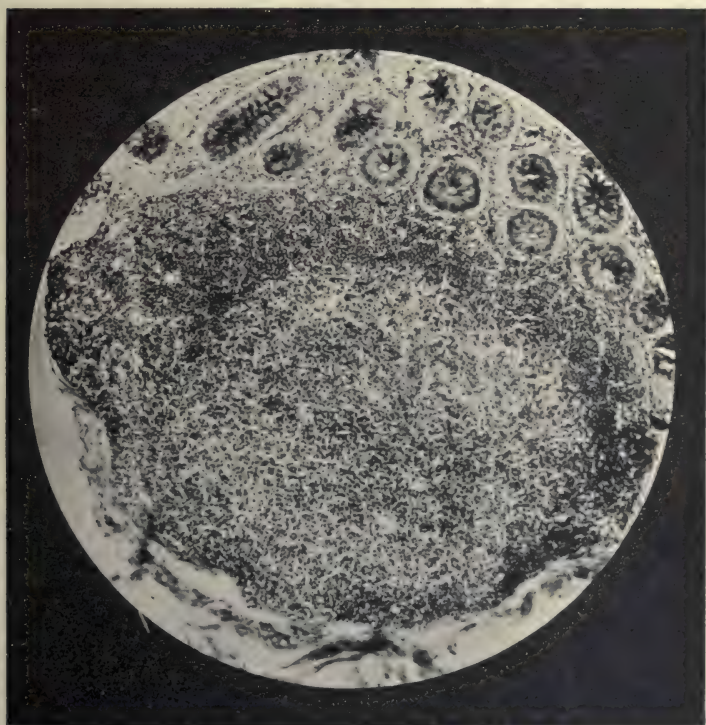


FIG. 145.—A LYMPHATIC NODULE, SOLITARY FOLLICLE, FROM THE LARGE INTESTINE OF MAN.

In the upper part of the figure the edge of the intestinal mucosa is shown; it contains many secreting tubules which have been cut in transverse or oblique section and are lined by columnar epithelium and goblet cells. Photo. $\times 80$.

connective tissue. In those locations where it exists independently the follicle is completely surrounded by the connective tissue in which it lies. In other places, as in the lymphatic glands,

the follicle is only partially surrounded by the connective tissue trabeculæ of the organ. Not only do fine branches from the surrounding connective tissue bundles penetrate the periphery of the follicle, but the reticulum of the follicle is continuous with these trabeculæ, thus forming a supporting stroma in which the lymphatic corpuscles are embedded.

The lymphatic corpuscles are loosely packed in the center of the follicle, and in this portion cell division by mitosis is most active. This central portion is the *germinal center* of Fleming. The germinal center is surrounded by a denser circumferential layer of lymphoid tissue in which karyokinesis is less active. Between this denser portion and the surrounding connective tissue the lymphatic corpuscles are again more loosely packed, and over a greater portion of the follicle are separated from the trabeculæ by a lacuna-like space, the peripheral lymphatic sinus.

The follicle is usually supplied with a thin-walled artery, occasionally two, which penetrates to the middle of the follicle to form a wide meshed capillary plexus. The capillaries, at the periphery of the follicle unite to form two or more veins, which are contained in the adjacent connective tissue.

The *lymphatic corpuscles* are mostly of the mononuclear type of leucocyte, the small mononuclear or lymphocyte type being the most abundant. Polynuclear and acidophile leucocytes are also found in the lymphatic follicles, though in much smaller numbers. Mitosis is most frequently observed in the large mononuclear type. Because of the nomadic tendencies of the leucocytes the boundaries of the lobule are not always sharp, the lymphatic corpuscles frequently infiltrating the surrounding connective tissue so as to render it most difficult to distinguish the latter from the true lymphoid tissue of the follicle.

THE LYMPHATIC NODES (*Lymphatic Glands,* Lymphoglandulæ*).—These structures occur in the course of the lymphatic circulation in various parts of the body. They are found in the neighborhood of the large joints, as in the axilla, the groin, the popliteal space, in the prevertebral and mediastinal connective tissue of the abdominal and thoracic cavities, and in the mesentery. They are frequently in relation with the large arteries, e. g., the renal, internal and external carotids, etc.

* Since the lymphatic glands are in no sense true secreting glands after the manner of the serous and mucous secreting glands, this name is most ill-chosen.

Each lymphatic node consists of a mass of follicular lymphoid tissue inclosed within a fibro-elastic connective tissue capsule. The capsule also contains a little smooth muscle tissue, but this is never so abundant as to form any considerable portion of the fibrous membrane; in fact, as compared with the somewhat similar capsule of the spleen, that of the lymphatic node is notably deficient in smooth muscle.

An *afferent lymphatic vessel*, pursuing its course within the capsule, enters the lymphatic node by a number of subdivisions which penetrate the deeper layers of the capsule and open into a

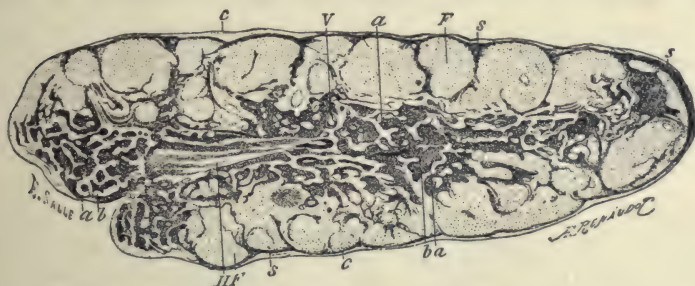


FIG. 147.—TRANSECTION OF A CERVICAL LYMPHATIC NODE OF A DOG.

The denser portions of lymphoid tissue are light in the figure. *a*, medullary cord of dense lymphoid tissue; *b*, looser lymphoid tissue of the cavernous medulla; *c*, capsule; *F*, dense lymphoid follicle of the cortex; *HF*, fibrous tissue containing the large vessels of the hilum; *s*, peripheral lymphatic sinus; *V*, blood vessel. Magnified several diameters. (After Ranvier.)

peripheral lacunar space, the *lymphatic sinus*, which separates the inner surface of the capsule from the adjacent lymphoid tissue, but which is bridged across at frequent intervals by the fine strands of lymphatic reticulum.

The lymphoid tissue, which forms the substance of the node, consists of a dense peripheral portion, the *cortex*, formed by closely packed lymphatic follicles, and a looser *medulla* in which are columnar accumulations of dense lymphoid tissue, the lymphatic cords.

Cortex.—The follicles of the cortex are partially separated from each other by septum-like trabeculae which extend inward from the fibrous capsule, and along which the peripheral lymphatic sinuses are continued into the substance of the node to partially surround its lymphatic follicles.

Each lymphatic follicle is thus surrounded, except at its central pole, by a peripheral lymphatic sinus, into which the afferent lym-

phatic vessels pour their contents. The lymph on entering the gland is thus permitted to enter the spaces of the reticulum and percolate through the lymphatic follicles of the cortex before it can reach the looser portions of the medulla. Each of the follicles of the cortex contains a germinal center in which lymphatic corpuscles are actively formed by mitosis, and from which the leucocytes readily escape along the lymphatic channels of the reticulum into the more open meshes of the medulla.

Medulla.—The medulla occupies the center of the gland, and at one point, the hilum, it reaches the surface. At this point a considerable mass of fibrous trabeculae enters the medulla, carrying with it the larger blood vessels to be distributed to all portions of the gland. The finer ramifications of these medullary trabeculae are continuous with those of the cortex.

The lymphoid tissue of the medulla is divisible into the denser branching *lymphatic cords*, in which the leucocytes are closely

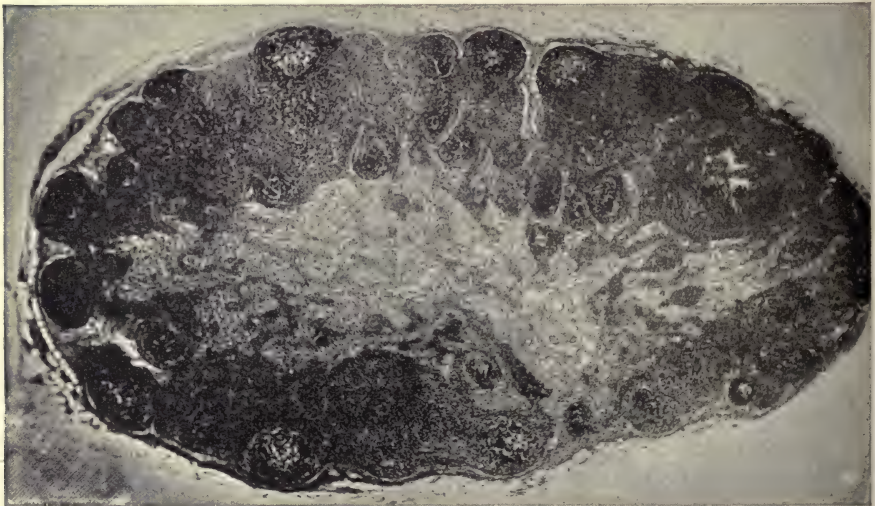


FIG. 148.—TRANSECTION OF A MESENTERIC LYMPHATIC NODE OF MAN.

Hematein and eosin. Photo. $\times 38$.

packed, and the intervening *pulp spaces*, in which leucocytes are less numerous, and the reticulum of which is continuous with that of the cortical follicles.

The pulp spaces are broad channels, which are occupied by a reticulum whose meshes are partially filled with lymphatic cor-

puscles. They are bounded by a layer of endothelioid cells which everywhere incloses the denser lymphatic cords. The function of these cords would seem to be comparable to that of the peripheral lymphatic follicles.

The pulp spaces are open toward the cortex, whence they receive the afferent lymph after it has percolated through the follicles, but toward the hilum the spaces are continued into the efferent radicles of the lymphatic vessels which, in the connective tissue of this part, unite into larger trunks, and finally form several efferent, lymphatic vessels of considerable size.

The *reticulum* of the lymphatic gland is a close-meshed network of interlacing fibrillar bundles, which are here and there clasped by flattened endothelioid connective tissue cells. Reticulum is but poorly stained with either acid or basic dyes, is destroyed by acids and bases, but is not digested by pancreatin. After prolonged action of Weigert's specific stain for elastic tissue it is but slightly colored.

Lymphatic Corpuscles.—The great majority of these cells are of the small mononuclear or lymphocyte type. Large mononuclear cells with a considerable cytoplasmic body are also very numerous. Polynuclear neutrophile leucocytes, though of frequent occurrence, are less abundant than the previous varieties. Eosinophile cells are present in small numbers, and large basophilic mast-cells are occasionally seen, though according to Carlier * they are mostly confined to the connective tissue. Drummond † also found large multinuclear giant cells, megakaryocytes, similar to those of the bone marrow; these were, however, very rare.

Many of these cells, after proper fixation, show mitotic figures. This mitosis has been most frequently observed in the large mononuclear type, and is most abundant in the germinal centers of the follicles. The small mononuclear and polynuclear types have also been shown to be capable of cell reproduction by indirect division. Reproduction by direct division of leucocytes appears to be rare, if indeed it ever actually occurs.

The mononuclear as well as the polynuclear forms appear to be phagocytic. Among the inclusions which have been found within these cells are fat globules, pigment granules, red blood corpuscles in partial disintegration, insoluble pigments, such as carbon granules, etc., and bacteria.

* J. Anat. and Physiol., 1893.

† J. Anat. and Physiol., 1900.



FIG. 149.—DIAGRAM OF THE BLOOD VESSELS OF A LYMPHATIC NODE.

A composite section of three follicles and the medullary cords of a mesenteric lymphatic node of the dog. *A*, artery; *B*, medullary artery; *C*, follicular vein; *E*, artery going to the capsule; *F*, capillaries in the periphery of a cord; *G*, medullary vein; *H*, follicular artery; *I*, arterial capillaries in a follicle; *J*, vein from capsule; *K*, cord; *L*, trabecula; *V*, vein. $\times 501$. (After Calvert.)

Blood vessels.—The arteries enter the lymphatic node at its hilum, and, following the trabeculæ within which they lie, are distributed to all portions of the organ. In the medulla branches are distributed to the lymphatic cords, in which they form a wide-meshed capillary plexus.

The terminal branches of the primary divisions of the afferent artery are distributed to the follicles of the cortex. A single follicular branch (Calvert*) enters the follicle and passes straight toward its center, where it breaks into a plexus of divergent capillaries which unite at the surface of the follicle to form small venous radicals.

The veins follow the interfollicular trabeculæ in their course toward the medulla, where they enter the medullary trabeculæ, are augmented by venous radicals from the capillary plexuses of this portion of the gland, and thence follow the trabeculæ to the hilum, where they unite to form the efferent vein.

Certain of the arteries also pass from the medulla through the interfollicular trabeculæ to the capsule of the gland, to which they supply a capillary plexus. The blood is returned through veins which retrace the course of the arteries and enter the large veins of the medullary trabeculæ.

HEMOLYMPH NODES.—These structures, which closely resemble the lymphatic nodes, were first described by H. Gibbs,† in 1884. He found them in the connective tissue, between the renal artery and vein, in the human subject. They have since been found in the prevertebral connective tissue, and in the mediastinum and mesentery. They are larger and more numerous in the ruminants, ox, sheep, etc., than in man. Their size varies from that of a millet seed to that of a pea. In color they closely resemble a minute extravasation of blood.

These organs are essentially lymphatic structures in which the lymphoid tissue is arranged in the form of cords rather than in follicles. The node is inclosed by a fibrous capsule, beneath which is a broad sinus filled with blood. In this fact lies the chief distinguishing feature of these glands.

The *peripheral blood sinus*, which is analogous to the peripheral lymphatic sinus of a lymphatic node, sends into the interior of the organ a greater or less number of secondary sinuses. Based largely upon the abundance of these secondary sinuses, the hemo-

* Anat. Anz., 1897.

† Quart. J. Mic. Sc.

lymph nodes have been divided into two varieties, which were named by Warthin* the "*spleenolymph glands*" and the "*marrowlymph glands*."

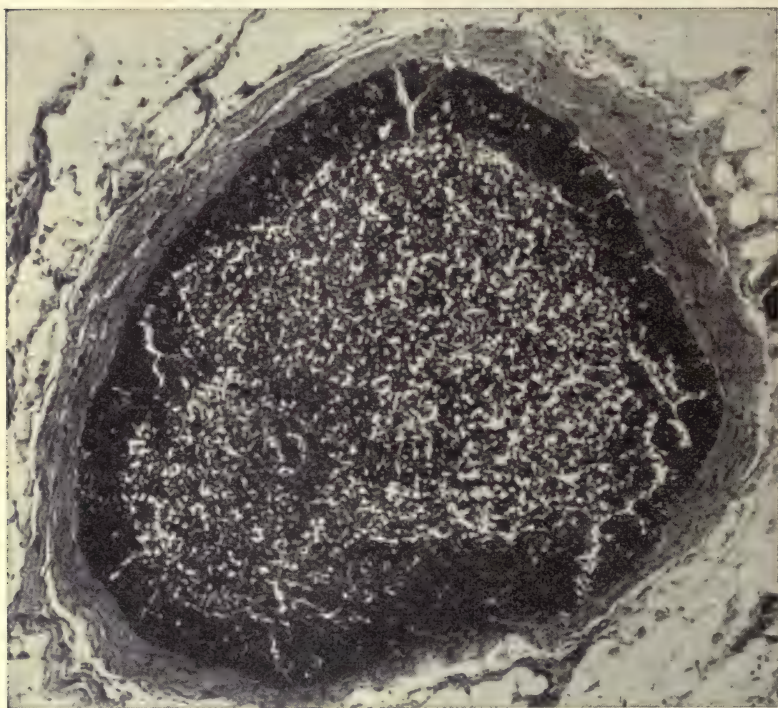


FIG. 150.—HEMOLYMPH NODE OF THE SHEEP.

The dark areas are blood sinuses; the lighter portion within is lymphoid tissue.

Photo. $\times 35$. (After Warthin.)

In the spleenolymph type, which is the more abundant, the gland is of small size and is well filled with secondary blood sinuses. The lymphoid tissue is supported by a similar reticulum, and contains the same varieties of lymphatic corpuscles as in the lymphatic nodes.

In the marrowlymph glands a somewhat similar structure is found. The blood sinuses are less numerous and lymphatic follicles do not occur (Vincent, Warthin). The eosinophile leucocytes are more numerous than in the spleenolymph type, and the marrowlymph glands as a rule are the larger.

* J. Bost. Soc. Med. Sc., 1901.

Intermediate types between the lymphatic nodes and the spleenolymph (Vincent*) on the one hand, and between the spleenolymph gland and the spleen and marrowlymph type on the other hand, are of frequent occurrence.

Blood supply.—The afferent artery, according to Drummond,† enters the hilum with the connective tissue, and through the trabeculæ reaches all parts of the gland. In the lymphoid tissue its branches form a capillary plexus whose vessels open into the blood sinuses. All the sinuses, peripheral and secondary, communicate with each other, and from them the blood is ultimately collected into two or more thin-walled veins. In the center of the gland these vessels unite to form an efferent vein which passes out at the hilum.

THE TONSIL (*the Faucial Tonsil, Palatine Tonsil, Amygdala*).—The tonsil consists of a mass of *lymphoid tissue* which projects slightly from either side into the cavity of the fauces, and is cov-

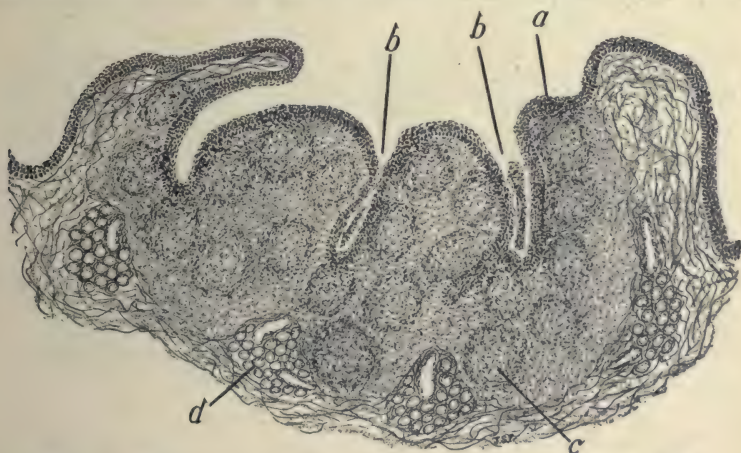


FIG. 151.—HORIZONTAL SECTION THROUGH THE FAUCIAL TONSIL OF A CHILD.

Semi-diagrammatic. *a*, stratified epithelium; *b*, crypts; *c*, lymphoid nodule; *d*, mucous-secreting gland. Hematein and eosin. \times about 20.

ered by a layer of *stratified epithelium* continuous with that which lines the oral and pharyngeal cavities. The lymphoid follicles which compose the tonsil immediately underlie the epithelial coat, and are embedded in areolar connective tissue.

The epithelial coat here and there penetrates the substance of

* J. Anat. and Physiol., 1897.

† J. Anat. and Physiol., 1900.

the organ in the form of invaginated funnel-shaped depressions, the *crypts* ("follicles" of the tonsils). The ducts of many mucous glands open into the recesses of these branching crypts. The mucus secreting glands lie in the loose connective tissue which surrounds the tonsil on all but its faucial surface. The crypts are lined throughout by a layer of stratified epithelium, which is continuous with that on the free surface of the tonsil, but which becomes progressively thinner as it recedes into the deeper recesses of the crypts.

Many of the lymphatic corpuscles migrate into the intercellular spaces of the epithelial layer, and even penetrate to the free surface; thus they find their way into the oral cavity, where they are found in large numbers in the saliva, as "*salivary corpuscles*." If such salivary corpuscles are examined in a drop of saliva, freshly prepared, the fine intracellular granules of the polynuclear leucocytes will be seen to undergo an active dancing movement, *Brownian motion*. The salivary corpuscles are derived not only from

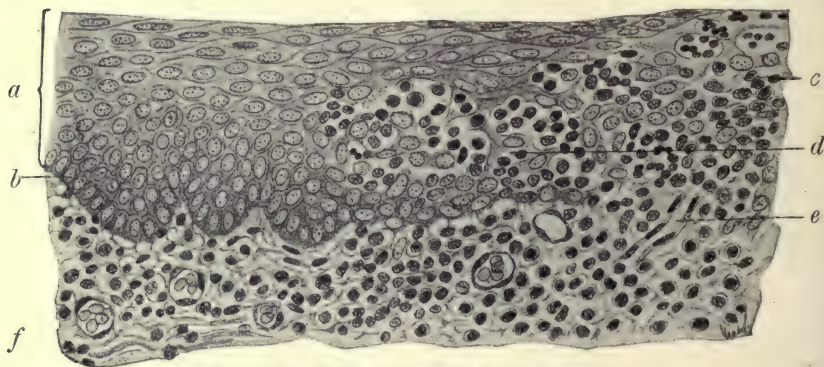


FIG. 152.—FROM A CRYPT OF A DOG'S TONSIL.

a, stratified epithelium; *b*, basal margin of the epithelium; *c*, infiltration of the epithelium by leucocytes; *d*, spaces in the epithelium filled with leucocytes and epithelial cells; *e*, blood vessel; *f*, lymphoid tissue. $\times 150$. (After Böhm and von Davidoff.)

the faucial tonsils but from the other lymphoid tissue which is in relation with the oral mucous membrane, e. g., the lingual and pharyngeal tonsils.

The passage of leucocytes through the epithelial surface of the faucial tonsil is so very active that at times the epithelium becomes completely filled with these cells, and it is then difficult to distinguish it from the adenoid tissue beneath.

The Lingual Tonsil.—A collection of lymphatic follicles is also found at the base of the tongue in the median line, between the circumvallate papillæ and the epiglottis. This, because of its



FIG. 153.—THE LINGUAL TONSIL OF MAN.
a, a crypt; b, von Ebner's glands. Hematein and eosin. $\times 45$.

similarity in appearance and in structure to the faucial tonsil, is called the lingual tonsil.

In the lingual tonsil, however, the follicles are grouped about a single wide-mouthed crypt, the *foramen cæcum lingui*. This crypt is frequently branched, and into it the many mucous glands of the neighboring lingual mucosa pour their secretion.

The Pharyngeal Tonsil.—The posterior wall of the naso-pharynx is supplied with a similar accumulation of lymphatic follicles, the pharyngeal tonsil. It lies in the median line and extends downward from between the orifices of the Eustachian tubes for a distance of three centimetres (Klein). It contains a considerable number of lymphatic follicles and several small crypts.

The pharyngeal tonsil is prone to hypertrophy in youth, in which case it forms the adenoid growths which are so common in strumous children.

THE THYMUS.—The thymus is an organ of fetal and infantile life, attaining its maximum development during the second year

of childhood. After this time it is gradually replaced by adipose tissue, its retrograde metamorphosis becoming complete at about the age of puberty.

At its maximum the thymus forms a large lymphoid mass, embedded in areolar connective tissue, the trabeculae of which divide the organ into several lobes and innumerable minute *lobules*. Each lobule is surrounded by a thin fibrous capsule, by which it is loosely united to its neighbors.

The lobule consists of a mass of lymphoid tissue, which is dense at the periphery but looser in the central portion. It is thus divisible into a dense cortex and a loose medulla, both composed essentially of lymphoid tissue, but between which, because of the difference in density, there is a sharp line of demarcation. Frequently, at some point on its circumference, the medulla reaches

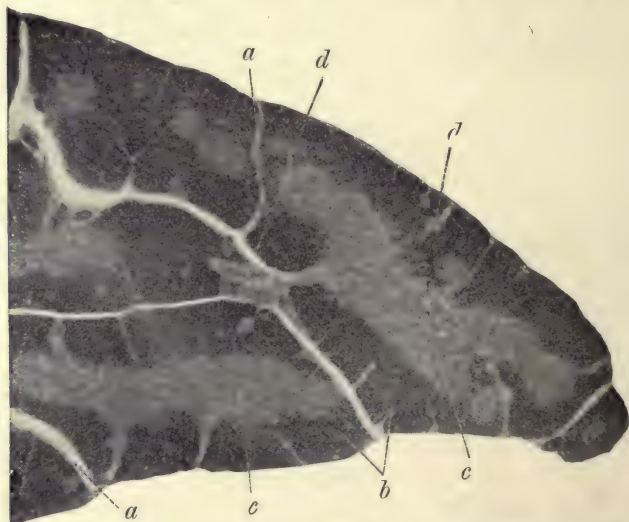


FIG. 154.—A SECTION THROUGH SEVERAL LOBULES OF THE THYMUS OF AN INFANT.

a, loose fibrous septum between the lobules; *b*, cortex, and *c*, medulla of the lobule; *d*, blood vessels in the connective tissue. Hematein and eosin. Photo. $\times 60$.

the surface of the lobule, and at such locations a narrow column of medullary lymphoid tissue connects it with the adjoining lobule.

A close-meshed reticulum, within the narrow meshes of which are closely packed lymphatic corpuscles, composes the lymphatic tissue of the lobule. That of the cortex and the medulla is alike,

except for the fact that the meshes of the reticulum in the cortex are much more crowded with leucocytes than are those of the medulla. The medulla of each lobule is also characterized by the presence of several groups of concentrically arranged epithelioid cells, the *concentric corpuscles of Hassal*.

Each concentric corpuscle consists of a large central cell or group of cells, which is surrounded by two to five layers of concentrically arranged flat epithelioid cells. These groups or cell nests are strongly acidophile in their staining reactions, and therefore stand out

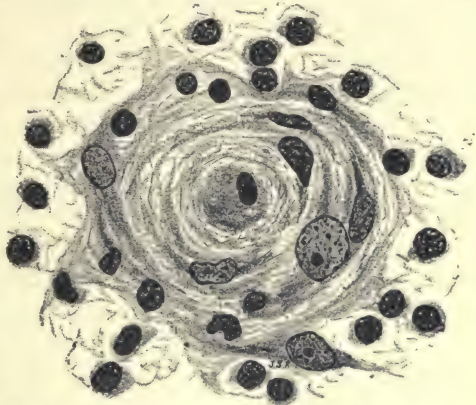


FIG. 155.—A CORPUSCLE OF HASSAL FROM THE THYMUS OF AN INFANT.

Hematein and eosin. $\times 665$.

in marked contrast to the basophilic nuclei of the surrounding lymphoid tissue. Since no similar structure occurs elsewhere in the body, the concentric corpuscles are absolutely characteristic of the thymus lobule.

The nature of the concentric corpuscles is not satisfactorily understood. According to one hypothesis they represent blood vessels whose lumen has been obliterated by proliferation of its endothelial cells. Another theory regards them as remains of the epithelial columns from which the organ arises in the embryo.

The *types of lymphatic corpuscle* which are found in the thymus are similar to those of the lymphatic glands, though polynuclear leucocytes are rather more frequent here, and giant cells, polynuclear or multinuclear in form, may be readily found in the medulla of this organ. Eosinophile cells have been found in the thymus even at a very early period of embryonic life (Schaffer*), and Beard† has ascribed the first formation of embryonic leucocytes to this organ.

Blood supply.—The larger arteries of the thymus are distributed within the interlobular connective tissue. They supply branches

* Centralbl. f. d. med. Wissensch., 1891.

† Lancet, 1899; and Anat. Anz., 1900.

to the lobule which penetrate to the medulla, where they form a plexus of sinusoidal capillaries with elongated meshes, and also distribute radiating capillaries to the cortical portion of the lobule. These sinusoidal vessels are highly characteristic of the medulla of the thymus lobule. They unite to form venous radicals of considerable caliber, which leave the lobule to join the interlobular veins in the loose connective tissue between the lobules.

Lymphatic vessels are of frequent occurrence in the interlobular connective tissue, and their branches occasionally penetrate to the medulla of the lobule. Small nerve trunks are also found in the interlobular connective tissue, but seem to be chiefly distributed to the walls of the larger blood vessels.

THE SPLEEN.—The spleen contains a pulp which closely resembles adenoid tissue, and is surrounded by a well-developed, fibro-muscular capsule. The spleen pulp, as indeed the entire structure of the organ, is intimately related to its blood supply.

The framework of the organ includes a capsule, numerous trabeculæ, and a delicate reticulum. The spleen is also inclosed by a reflection of the peritoneum which supplies a serous coat to all portions of the surface of the organ, except at the attachments of the gastro-splenic omentum and the phreno-splenic and lieno-renal ligaments.

The capsule of the organ, to which its serous coat is loosely attached, comprises two layers, an outer fibrous and an inner muscular. In some animals—e. g., the ox—these layers are much more highly developed than in man. The outer layer consists of dense interlacing bundles of fibrous tissue, in which is an abundant network of elastic fibres. The inner layer contains, in addition to the fibro-elastic membrane, a considerable amount of smooth muscle which forms interlacing bundles. In the ox, in which animal this coat is most highly developed, two layers, the fibres of which cross each other at right angles, may be distinguished in the muscular portion of the capsule.

From the inner surface of the capsule **trabeculæ** extend into the interior of the organ and penetrate to all its portions. These trabeculæ consist of fibrous and elastic tissue, with which bundles of smooth muscle fibres are intermingled. At the hilum a large mass of trabecular tissue is carried into the interior of the organ along with the larger blood vessels. Those trabeculæ which arise in this manner serve as sheaths for the larger arteries and veins.

From the borders of the trabeculae, as well as from the inner surface of the capsule, a delicate **reticulum** is continued into the spleen pulp. This reticular tissue is similar in structure to that

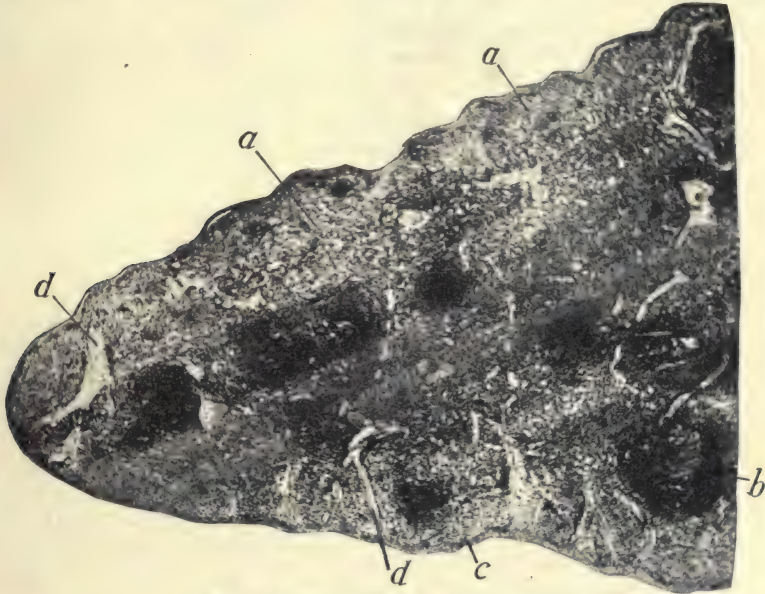


FIG. 156.—FROM THE SPLEEN OF A CHILD.

a, splenic pulp; b, Malpighian corpuscle; c, capsule; d, vascular trabeculae. Hematein and eosin. Photo. $\times 28$.

of the lymphatic glands though consisting of rather coarser fibrous bundles. Mall* states that the splenic reticulum is readily dissolved in acids and alkalis, but that, unlike that of lymphoid tissue, it is also digested by pancreatin. The meshes of this reticulum are occupied by the splenic cells.

Splenic cells.—Besides the endothelioid cells of the reticulum and the epithelium of the small blood vessels, the following cell types can be distinguished in the splenic pulp.

1. *Large mononuclear leucocytes.* These are the most numerous of the several cell types of the spleen. They possess a broad rim of cytoplasm, and frequently exhibit karyokinetic figures.

2. *Small mononuclear leucocytes* or *lymphocytes*, with a deeply staining nucleus and narrow cytoplasmic rim.

* Johns Hop. Hosp. Bull., 1898.

3. *Polynuclear neutrophile leucocytes*, similar to those of the blood.

4. *Eosinophile leucocytes*, with numerous coarse acidophile granules and a polylobular nucleus. This variety is more frequent than in any other lymphoid tissue except the bone marrow.

5. *Basophile leucocytes*, mononuclear or polynuclear, but with a considerable basophilic rim of cytoplasm.

6. *Phagocytes*, either mononuclear or polynuclear, with a broad ring of cytoplasm, within which are found coarse pigment granules, fragments of disintegrated red blood cells and even entire blood corpuscles, fat droplets, and in diseased conditions bacteria.

7. *Giant cells, megakaryocytes*, with a polylobular nucleus and a very broad rim of cytoplasm. Red blood corpuscles and fat droplets have also been found in these cells.

8. *Red blood corpuscles*, erythrocytes, occur in great abundance; they are derived from the blood. They are found not only within the thin-walled vessels of the pulp but also in the spaces of the reticulum, where, if the slightest congestion of the organ is present, they are so numerous as to outnumber the other cell types.

9. *Nucleated red blood corpuscles, erythroblasts*. The embryonic spleen contains true "blood islands" in which erythroblasts are actively formed. In the normal spleen of adult man, as well as of other mammals, nucleated red blood cells appear to be quite constantly present, though in relatively small numbers.

10. *Blood platelets*, thrombocytes and thromboblats, are of frequent occurrence. They are probably derived from the blood.

Blood supply.—The further structure of the spleen is closely connected with its blood supply.

The *arteries* enter the hilum of the organ in a group, and following the branching trabeculae reach all portions of the organ. The arterial bifurcations are not always coincident with the subdivision of a trabecula, so that the latter, instead of including a blood vessel, form solid columns of fibro-muscular tissue.

The wall of the trabecular arteries of the spleen is rich in smooth muscle, the fibres of which are circularly disposed. The adventitia is loose, thin, and firmly adherent to the substance of the trabecula in which the vessel lies: it contains a system of perivascular lymphatics and tissue spaces.

The smaller branches of these arteries finally leave the trabeculae to pass directly into the spleen pulp. Within this tissue their muscular coat becomes much thinner, and their adventitia is re-

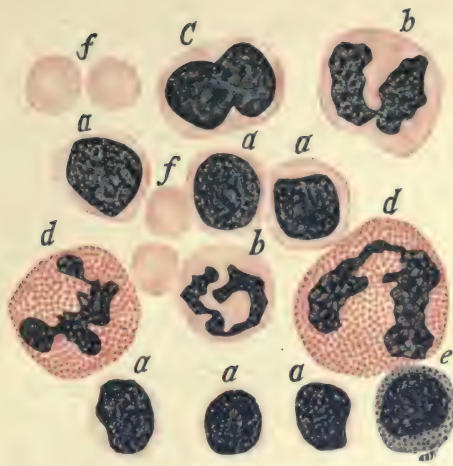


FIG. 157.—TYPES OF CELLS FROM A SMEAR PREPARATION OF THE PULP OF THE HUMAN SPLEEN.

a, lymphocytes; *b*, polynuclear neutrophile leucocytes whose granules are not stained by the method used; *c*, large mononuclear leucocyte; *d*, eosinophile cells; *e*, basophile cell; *f*, red blood cells. Hematein and eosin. $\times 1200$.

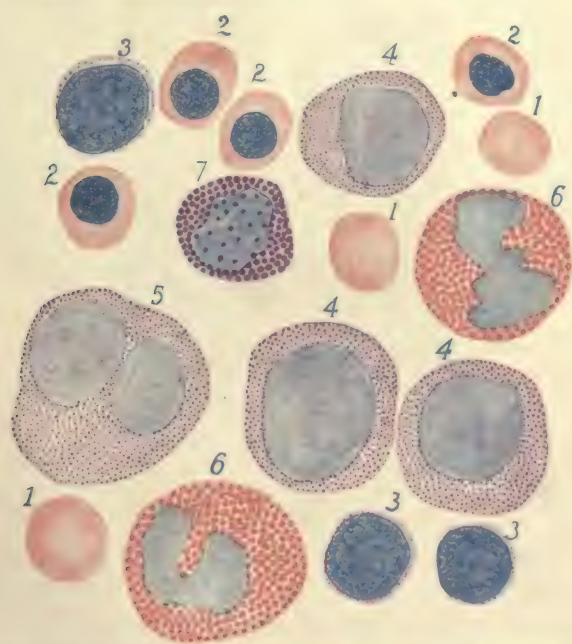


FIG. 158.—TYPES OF CELLS FROM A SMEAR PREPARATION OF THE MARROW OF A HUMAN RIB.

1, red blood cells; 2, nucleated red blood cells, erythroblasts; 3, lymphocytes; 4, large mononuclear cells with neutrophilic granules; 5, polynuclear neutrophile; 6, eosinophile cells; 7, a basophile cell. Eosin and methylen blue. Noeh's stain. $\times 1200$.

placed by an investment of *adenoid tissue*. In the spleen pulp of some animals the adenoid tissue forms a complete investment of considerable thickness with occasional slender fusiform enlargements. In other mammals and in man this sheath is incomplete, but here and there forms ovoid accumulations of lymphoid tissue, the *Malpighian corpuscles*, which inclose the arterial twigs. These

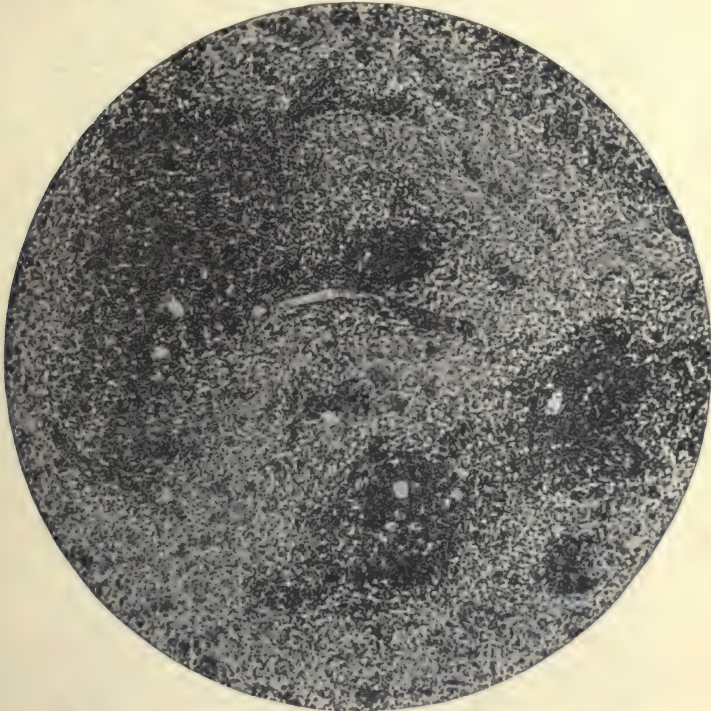


FIG. 159.—THREE MALPIGHIAN CORPUSCLES OF THE HUMAN SPLEEN.

Each lymphoid nodule contains one or more arterioles; a branch of one of these is seen in longitudinal section. Hematein and eosin. Photo. $\times 338$.

lymphatic follicles are eccentrically placed as regards the artery, and are most frequently situated at the bifurcations of the vessel. They differ from the lymphatic follicles of other organs in that they frequently contain no germinal center, and invariably possess one or more small arteries with distinct muscular walls, which are rarely ever situated in the axis of the corpuscle. The Malpighian corpuscle is therefore characteristic of the spleen.

Within the Malpighian corpuscle the artery gives off capillary twigs which pass radially to the adjacent splenic pulp, and there enter the small veins. At the circumference they are in close relation with the *splenic ellipsoids*, which are formed by minute condensations of the splenic reticulum (Schäfer).

Within the Malpighian corpuscle also, or in the adjacent splenic pulp, the small artery breaks into a minute brush of terminal ves-



FIG. 160.—DIAGRAM OF A LOBULE OF THE SPLEEN.

A, artery lying in the center of the lobule; Am, a terminal ampulla of the artery; C, intralobular vein; L, a Malpighian corpuscle; P, venous plexus within the pulp of the spleen; Tr, fibro-muscular trabeculae within the lobule; V, interlobular vein, lying in a large trabecula. (After Mall.)

sels, the *penicilli* of Ruysch. The ultimate destiny of these vessels is still in doubt, some observers claiming that they open free into the reticular meshes of the splenic pulp, others that they form a system of closed capillaries within the pulp, by which the blood is transferred directly to the veins.

Mall* has shown that each terminal artery enters a lobular compartment which is partially outlined by coarser trabeculæ, and within which is a mass of spleen pulp supported by the finer trabecular processes and the still more delicate reticulum. This schematic structural unit he has termed the *lobule of the spleen*. The terminal artery enters its axis through that margin which is directed toward the hilum. Within the lobule the artery gives off its terminal twigs, which end in minute dilatations, the *ampullæ* of Thoma. From some of these end twigs, capillary spaces direct the blood current into the broad venous radicals. Elsewhere the blood seems to be poured directly into wide pulp channels, comparable to the sinuses of the lymphatic glands, by which the blood current under ordinary conditions is directed into the venules, but which under conditions of very slightly increased blood pressure permit the extravasation of considerable quantities of blood into the meshes of the surrounding splenic reticulum.

The *veins* begin as wide sinusoidal channels within the splenic pulp. At first, and for a considerable distance, they follow an independent course through the pulp, receiving at the same time frequent accessions of blood from other venous radicals. Finally, however, the veins enter the larger trabeculæ, but are still devoid of more complete coats than the thin membrane of fibro-elastic tissue which surrounds the endothelial tube, but which is now ensheathed by the trabecular tissue. Henceforth the path of the veins lies within the trabeculæ, and is directed toward the hilum. On approaching the hilum the larger veins acquire the usual venous coats. Having arrived at the hilum they form several efferent vessels which, in the outlying connective tissue, form by their union the splenic vein.

The spleen is poorly supplied with *lymphatics*. These vessels

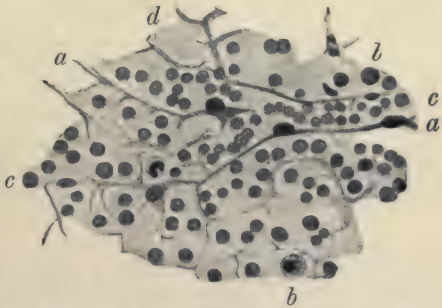


FIG. 161.—THE ORIGIN OF A VEIN IN THE SPLENIC PULP.

a, venous endothelium; b, leucocytes; c, red blood cells (appearing rather too dark in the reproduction); d, a mesh of the splenic pulp. Highly magnified. (After Bannwarth.)

form a plexus within the capsule and larger trabeculæ, and a perivascular plexus in the walls of the blood vessels.

The *nerves* of the spleen form a plexus of nonmedullated nerve fibres about the larger arteries at the hilum. From this plexus fine branches are distributed to the muscular tissue of the trabeculæ and to the arterial branches down to their finest ramifications. Nerve fibres have not as yet been demonstrated within the splenic pulp.

CHAPTER XI

BONE AND BONE MARROW

BONE is a firm calcareous tissue which is found only in the skeletal system. In the flat bones it forms a double layer of dense bony tissue between which is a narrow space, bridged across at frequent intervals and thus subdivided into a number of compartments, the marrow cavities. This central stratum presents a spongy appearance as compared with the denser periphery; it is therefore said to contain *spongy* or *cancellous bone*, while the more superficial lamellæ contain *compact bone*.

In the long bones a similar condition exists in the epiphyses, which consist of a wall of compact bone within which the marrow cavity is subdivided by bony partitions into numerous compartments; the epiphysis consists, therefore, of spongy bone. The shaft or diaphysis of the bone, however, contains a single large marrow cavity whose walls, except for a thin layer at either end, consist entirely of compact bone. A little spongy structure is present at either end of the shaft, in that portion which adjoins the marrow cavity.

The ends and facets of the bones are covered by a disk of hyaline cartilage, which forms the articulating surfaces of those bones which enter into the formation of the movable joints. These *articular cartilages* are peculiar in that they are not covered by a perichondrium, and their deeper cells, which adjoin the bone, are so arranged that their long axes are perpendicular to the free surface, as is the case in the central portion of free cartilaginous plates. Toward the free surface of the cartilage the long axis of the cell lies more nearly parallel to the surface, as is likewise the case at the surface of cartilaginous plates elsewhere. In the long bones of younger individuals a plate of hyaline cartilage is also found at the *epiphyseal lines* between the epiphyses and the diaphysis. This plate, which extends through the entire axis of the bone, becomes ossified later in life. It represents the line of

growth, and is the last portion of fetal cartilage to be transformed into adult bony tissue.

All those portions of the bone which are not covered by an articular cartilage are supplied with a membranous coat of fibrous tissue, the **periosteum**. The outermost layer of this membrane consists of interlacing bundles of dense fibrous tissue, in which are the larger blood vessels, whose branches are distributed to the underlying bone. The inner portion of this layer forms a firm fibro-elastic stratum, which in older individuals is closely attached to the surface of the bone. The periosteum of developing and growing bone, however, contains a third or innermost layer, in which are small blood vessels, fine connective tissue fibrils, and numerous small osteogenic cells, the osteoblasts. After growth of the bone has ceased, the deepest layer of the periosteum contains few small blood vessels and only occasional osteoblasts; these cells, however, are present in sufficient numbers to accomplish the regeneration of the bone after destruction of its osseous tissue. The medullary surface of the bone is likewise supplied with an osteogenic membrane of fibrous tissue, similar to the periosteum; it is known as the periosteum internum, endosteum, or *membrana medullaris*.

Compact bone, such as that composing the shafts of the long bones, consists of *concentric lamellæ* of calcified fibrous tissue, which constitute the *Haversian systems*, together with groups of parallel laminae, which are interposed between adjacent Haversian systems and are known as the *interstitial* or *ground lamellæ*. Many of the interstitial lamellæ are the remains of Haversian systems which have been partially absorbed during the development of the bone. In a section through the shaft of a long bone the Haversian systems are found in the middle of the wall, while superficial to them and just within the periosteum are a number of lamellæ which may be traced much or all of the way around the circumference of the cylindrical shaft, and which are known as the *outer circumferential lamellæ*. On the inner surface of the compact bony wall is a similar group of parallel laminae, which adjoin the marrow cavity, and are known as the *inner circumferential lamellæ*. In their finer structure the circumferential lamellæ are exactly similar to the cylindrical bony lamellæ of the Haversian systems.

An **Haversian System** contains a small central canal which is occupied by connective tissue, marrow cells derived from the marrow cavity during the process of development, small blood vessels,

nerve fibres, and perivascular lymphatics. Concentrically arranged around the Haversian canal are parallel layers of dense fibrous tissue, the *Haversian lamellæ*. The fibre bundles of this tissue form an interlacing network whose bundles frequently cross each other at right angles and whose interstices are occupied by a solid calcareous mass, con-

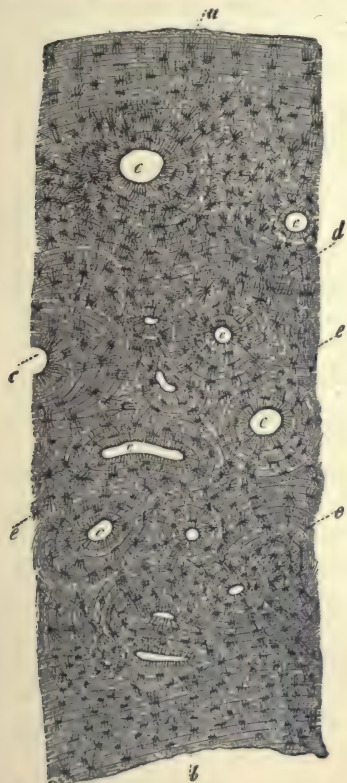


FIG. 162.—TRANSECTION THROUGH THE COMPACT BONY WALL OF A HUMAN METACARPAL BONE.

a, outer circumferential lamellæ; *b*, inner circumferential lamellæ; *c*, Haversian canals; *d*, interstitial lamellæ; *e*, lacunæ, with delicate radiating canaliculi. From a thin section of ground bone. $\times 90$. (After Kölliker.)

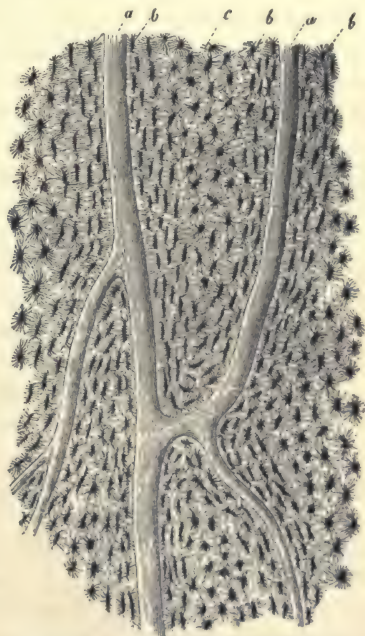


FIG. 163.—LONGITUDINAL SECTION OF GROUND BONE FROM THE SHAFT OF THE HUMAN FEMUR.

a, Haversian canals; *b*, lacunæ; *c*, canaliculi. $\times 100$. (After Kölliker.)

sisting chiefly of the phosphates and carbonates of calcium. From four to twenty such calcareous lamellæ are found in each Haversian system.

Both in and between the lamellæ are many small ovoid spaces which are partially filled by small flattened cells, the *bone corpuscles*: these spaces are known as the *lacunæ*. From each lacuna

minute canals, the *canaliculi*, radiate in all directions, thus placing the lacuna in open communication with its neighbors, and eventually with the lymphatic spaces of the central Haversian canal. The branching processes of the bone corpuscles frequently project for a short distance into the canaliculi. These cytoplasmic branches are more numerous in newly formed bone, later they are retracted and the corpuscles become more or less shriveled in appearance.

The Haversian system, being developed about a central canal which marks the course of a blood vessel, necessarily acquires a slender columnar shape, its long axis being usually disposed in a direction nearly parallel to that of the bone of which it forms a part. The Haversian canals frequently branch to permit a corresponding division of their blood vessels, and all of the Haversian canals are connected either directly or indirectly with the periosteum, the nutrient foraminæ, or the marrow cavity, from the blood vessels of which their vascular supply is derived.

The **interstitial lamellæ** are likewise composed of dense interlacing bundles of calcified fibrous tissue, within and between which are lacunæ, canaliculi, and bone corpuscles, all disposed in a manner exactly similar to their arrangement within the concentric lamellæ of the Haversian systems. Coursing through the interstitial lamellæ are *Volkman's canals*, which are similar in origin, contents, and function to the Haversian canals but which are not surrounded by concentric lamellæ. Volkman's canals frequently arise as branches of the Haversian canals which wander out, as it were, into the interstitial lamellæ.

The **circumferential lamellæ** do not differ in structure from the other bony lamellæ. They possess the same arrangement of laminated calcareous connective tissue, with lacunæ, canaliculi, and bone corpuscles, as in the concentric and interstitial lamellæ. Even more than elsewhere, however, the circumferential lamellæ are firmly bound together by elastic fibres which pass from the periosteum into and through the superficial lamellæ; these are known as the *perforating fibres of Sharpey*. Similar fibres connect together the concentric and interstitial lamellæ. The perforating elastic fibres are frequently surrounded by an envelope of fibrous connective tissue.

BONE MARROW.—Bone marrow consists of a variety of connective tissue which is rich in fat cells and blood vessels and which also contains osteogenic and hematopoietic elements, the

marrow cells. According to the relative proportion of these elements marrow is said to present two types, the yellow and the red marrow. The yellow marrow consists almost entirely of fat, with only occasional bands of true marrow tissue. The red marrow contains very little fat, but is so abundantly supplied with blood and marrow cells as to closely resemble a very vascular lymphoid tissue. The embryonic medulla of all bones contains fetal red marrow, but in later life the larger masses in the medulla of the shafts of the long bones is, in man, changed to the yellow variety. The red marrow, however, persists in the epiphyses of the long bones and in cancellous bone generally; it is especially characteristic of the marrow cavities of the ribs, vertebræ, base of the skull, and sternum.

Red marrow consists of fibrous and reticular tissues which are infiltrated by marrow cells and richly supplied with small blood vessels. The smaller veins possess exceedingly thin walls; in fact, these are so delicate that it is almost impossible to determine whether or not their endothelium, as also that of the capillaries, may be occasionally absent, thus placing the blood stream in direct communication with the pulp of the bone marrow.

The following types of **MARROW CELLS**, together with the fibrous connective tissue, reticulum, and blood vessels, make up the structure of red marrow (Figs. 158 and 164).

1. **Myelocytes** (*Marrow Cells Proper*).—These cells closely resemble the lymphatic corpuscles and the leucocytes of the blood, and, like them, include several cell types:

A. *Lymphocytes*; small cells with an ovoid deeply staining nucleus, and a very narrow rim of non-granular, faintly basophilic cytoplasm.

B. *Large mononuclear marrow cells*; whose ovoid nucleus stains faintly and is sometimes indented or constricted; their broad rim of non-granular cytoplasm is slightly stained by basic dyes. Occasionally the cytoplasm contains a scanty supply of very fine granules; rarely, also, the nucleus consists of two ovoid lobes which are united by a coarse chromatin filament (Jolly*).

C. *Polynuclear neutrophile marrow cells*; the nucleus of these cells is polymorphous and stains deeply; their cytoplasm forms a broad rim in which are many fine neutrophile granules. The cells of this variety, as well as those of the preceding, have been frequently found to possess centrosomes and mitotic figures.

* Arch. d'anat. mic., 1900.

D. *Eosinophile marrow cells*; cells of this type possess a broad rim of coarsely granular cytoplasm, the granules of which are strongly acidophile. Their nuclei differ from those of the corresponding cells of normal blood, since in the marrow they may possess either a single ovoid nucleus, a polymorphous nucleus, or they may be distinctly multinuclear, in which latter case the nucleus consists of two or more discrete ovoid chromatin masses.

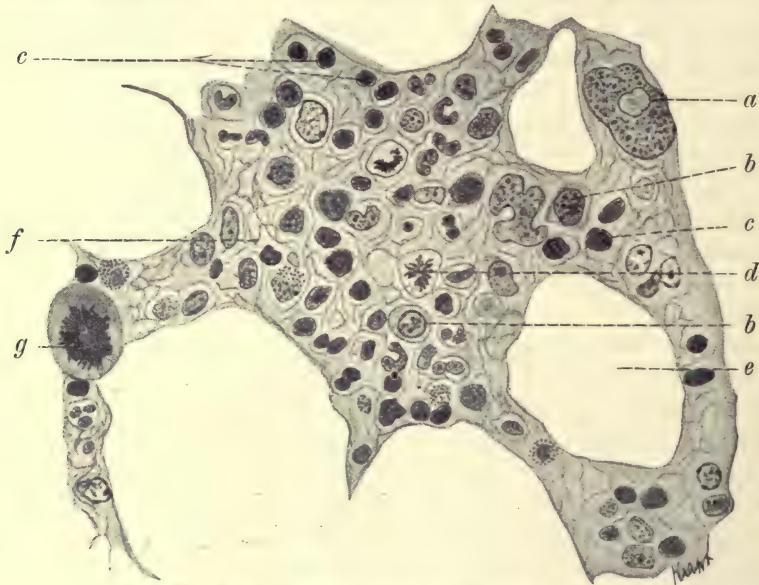


FIG. 164.—FROM A SECTION OF RED MARROW OF A HUMAN BONE.

a, giant cell; *b*, leucocytes; *c*, nucleated red blood cells; *d*, mitosis in a marrow cell; *e*, outline of a fat cell; *f*, reticulum; *g*, mitosis in a giant cell. $\times 680$. (After Böhm and von Davidoff.)

Many of the myelocytes are undoubtedly derived from the circulating blood, though most of them arise in the marrow by mitotic division of parent cells of the same type.

2. **Mast Cells.**—These cells are somewhat larger than the myelocytes. Their cytoplasm contains a number of coarse basophile granules, and their nucleus is of the polymorphous type. They are undoubtedly formed within the marrow, and probably arise by indirect division of similar cells.

3. **Giant Cells or Myeloplaxes.**—These cells are of extremely large size (30 to 100μ). They consist of an expansive mass of finely granular cytoplasm, and are either polynuclear or multinu-

clear. Howell* distinguished two varieties of these cells, the *polykaryocyte* and the *megakaryocyte*. The former is a large multinuclear cell, often containing as many as fifteen or twenty nuclei, which is especially characteristic of developing bone, and is identical with the so-called *osteoclasts*. These cells have usually been considered as possessing an intimate connection with the absorption of bone during its development and regeneration. The megakaryocyte is also a large cell but possesses a polymorphous nucleus, its many lobules being often arranged in a ring-like manner. These cells are relatively more abundant in the marrow of mature bone, and are usually found lying free in the marrow cavity rather than in contact with its walls, as is the case with the polykaryocyte.

Giant cells are probably derived from the leucocytes by a rapid growth of the latter, accompanied by endogenous division of the nucleus. The mature cells of this type reproduce themselves by mitosis.

Many of the giant cells contain particles of foreign matter and fragments of hemoglobin-containing protoplasm. Even whole red blood cells have been found within them. The giant cells have therefore been thought to take some part in the formation of red blood cells. Whether this hypothesis be true or not, the megakaryocyte variety is characteristic of the blood-forming organs, and is also found in the fetal liver and spleen during the period of their hematopoietic activity.

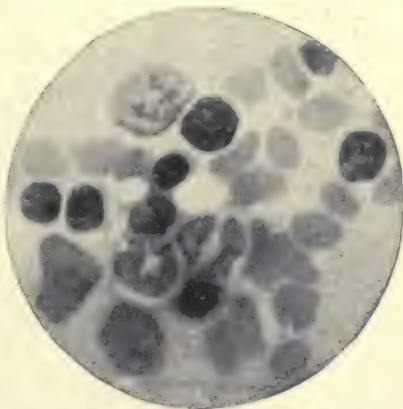


FIG. 165.—A GROUP OF CELLS FROM THE RED MARROW OF A HUMAN RIB.

Eosin and methylen blue, Nocht method.
Photo. $\times 1500$.

4. **Nucleated Red Blood Cells** (*Erythroblasts of Löwit* †).—These cells possess a hemoglobin-containing cytoplasm and a small, spherical, very deeply staining nucleus. Most of them are of about the size of the red blood corpuscle, *normoblasts*; others, *microblasts*, are somewhat smaller; still others, *megaloblasts*, are larger than the red blood cells. Many of the erythroblasts contain cen-

* J. of Morph., 1890.

† Arch. f. mik. Anat., 1891.

trosomes and centrosphere, and reproduce themselves by mitosis. Their nucleus finally disappears either by extrusion or by karyolysis, and in this way mature red blood cells are formed. Under normal conditions this process is confined to the marrow, but in certain diseases, and also in the healthy infant, a few erythroblasts escape into the blood current prior to the disappearance of their nucleus.

5. **Red Blood Corpuseles** (*Erythrocytes*).—These cells differ in no wise from those of the blood, from which many of them, as well as some of the leucocytes, are derived. The walls of the smaller blood vessels of the marrow are pervious to the red as well as to the white blood cells. Many of the erythrocytes, however, are formed within the marrow by the erythroblasts. *Blood platelets* are also present in the marrow, and occur in such abundance as to suggest that they may arise during the nuclear karyolysis from the achromatic portions of the erythroblastic nucleus as described by Eisen.*

6. **Fat Cells**.—These cells arise by the fatty infiltration of the connective tissue cells, and their number is subject to great variation. In fetal red marrow they are scanty, but as growth and development proceed the proportion of fat cells progressively increases until in the shafts of most of the mature bones the fat greatly predominates over all other tissue elements; the bone is then said to contain yellow marrow.

7. **Osteoblasts**.—The marrow of developing bones contains large numbers of small round or ovoid cells which are specially concerned with the formation of bony tissue. They contain a single oval or spheroidal nucleus, and are distinguished with difficulty from the mononuclear leucocytes, except when they are characteristically arranged in a membranous coat upon the surface of the bony walls of the marrow cavities. These osteoblasts not only occur in fetal bone, but are also found beneath the periosteum, and in relation to the endosteum of the marrow cavity in mature bone.

In addition to the above types, Jolly† describes certain very small cells with a polymorphous nucleus and a clear cytoplasm which occur in the red marrow, and are possibly identical with the *leucoblasts* of Lowit.‡ These cells are thought to be early types of leucocytes.

* Proc. Cal. Acad. Sc., 1897; and Jour. Morph., 1899.

† Loc. cit.

‡ Loc. cit.

Blood Supply.—Marrow, and especially the red variety, is richly supplied with blood. The nutrient arteries penetrate to the marrow cavity of the bone and supply an abundance of small arteries to all portions of the medulla. The arteries terminate in broad capillary vessels whose wide lumen and delicate endothelial walls determine their character as *sinusoids*. It was formerly thought that the endothelial walls of these vessels were here and there deficient, and, although recent investigations discredit the former observations, the all-important fact remains, that the endothelial walls are pervious to both red and white blood cells, neither is this the only location where the red as well as the white cells may, under certain conditions at least, penetrate the endothelial walls of the blood capillaries.

Efferent veins return the blood from the sinusoidal capillaries of the marrow. These veins, as also those of the bony tissue, are not supplied with valves.

The **lymphatics** of bone occur in great abundance in the periosteum, and as perivascular spaces penetrate the canals of Havers and Volkman and thus reach the medullary cavity. The existence of lymphatics within the marrow, other than in the sheaths of the blood vessels, is doubtful.

The **nerves** accompany the blood vessels in all portions of the bone and marrow, and form a rich perivascular plexus which is distributed to the walls of the vessels; occasional side fibrils are also distributed to the marrow. Nerve endings have not been demonstrated in compact bone. In the periosteum terminal nerve fibrils are supplied to the musculature of the blood vessels, and other sensory fibrils end in Paccinian corpuscles.

DEVELOPMENT OF BONE.—Bone makes its appearance very early in fetal life. The long bones are mapped out by masses of fetal hyaline cartilage as early as the embryo begins to acquire its typical form. The entire skeleton, with the exception of the flat bones of the trunk and those of the vault of the skull and face, are thus primarily formed by plates of fetal cartilage. The process by which these cartilaginous plates are formed into bone is known as *intracartilaginous* ossification.

The flat bones, together with most of those of the face, are formed directly from the mesoblastic connective tissue without the intervention of cartilage. This method of bone formation differs somewhat from the above and is known as *intramembranous* ossification.

INTRACARTILAGINOUS OSSIFICATION.—This process begins with the formation of plates of hyaline cartilage whose shape corresponds more or less closely with that of the future bone. This type of **fetal cartilage** differs from the hyaline cartilage of the adult only in the irregular form and distribution of its cartilage cells.

Each plate of fetal cartilage is enveloped by a layer of pre-fibrous tissue, the fetal perichondrium. The outer portion of the fibrocellular layer is destined to become the *periosteum* of the future bone; its innermost portion contains many small round cells, which, from their intimate relation to bone production, are known as osteoblasts. The inner portion of the perichondrium forms the osteogenic layer of the future periosteum.

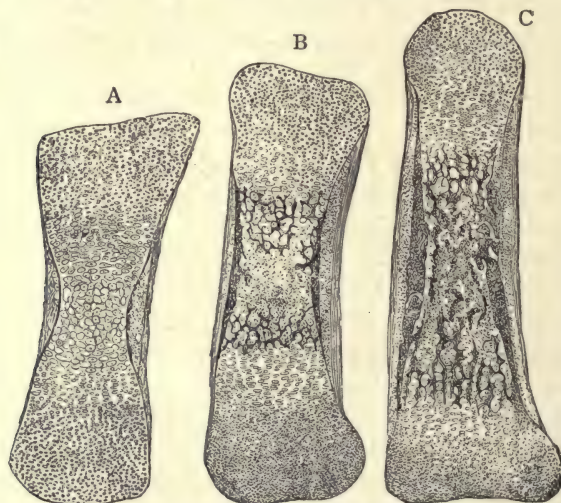


FIG. 166.—THE PRIMARY CHANGES IN INTRACARTILAGINOUS BONE FORMATION.

A, metatarsus; *B* and *C*, phalanges, of human embryo. In *A*, the earliest enlargement of cartilage cells at the center of ossification is shown. *B* and *C* are successively later stages. The bones are cut in longitudinal section. Carmin hematoxylin stain. $\times 27$. (After Toldt.)

Ossification of the cartilage begins at one or more points which are called **centers of ossification**. In the long bones, in which the process of bone formation can be most readily traced, there are usually three such centers, one near the middle of the cartilaginous plate, from which the diaphysis is formed, and one epiphysial center at each extremity. The centers for the epiphyses make their appearance much later than that for the shaft of the bone.

The first indication of beginning bone formation is evidenced by an **enlargement of the cartilage cells** which promptly arrange themselves in rows or columns that radiate from the center of ossification. This process is accompanied by absorption of the adjacent cartilage matrix, so that the enlarged cartilage cells are contained within broad spaces or *lacunæ*. The cartilage cells now appear to undergo a gradual but progressive absorption; their cytoplasm becomes shrunken and granular and finally disappears, even the nucleus at last succumbs to the process.

The absorption of the cartilaginous matrix proceeds more rapidly in those portions which separate the individual cells in the columns than in those other portions which intervene between the adjacent rows of cartilage cells. While the former portions are entirely absorbed, remnants of the latter remain, and in them calcium salts are deposited in an irregular manner. **Calcified cartilage**, the most primitive of the calcareous tissues, is thus formed.

The absorption of the cartilage matrix results in the formation of broad spaces into which osteogenic buds of primitive marrow tissue push their way from the perichondrium. Thus the **primordial marrow cavities** are formed. The fetal marrow which now occupies these cavities is derived from the osteogenic layer of the primitive periosteum. The osteogenous tissue of this layer, containing osteoblasts, osteoclasts, and developing blood vessels, grows into the cartilage in the form of bud-like cords which are preceded by absorption of the adjacent cartilage matrix. This so-called "eruptive tissue" promptly reaches the center of ossification and burrows its way into the enlarged cartilage *lacunæ* whose cells are now replaced by primary osteogenic marrow.

The *osteoblasts*, which thus gain access to the primary marrow cavities, now arrange themselves along the surface of the remnants of calcified cartilage and begin the deposit of the fibrous tissue and calcareous salts which compose the **primary bone**. Many of the osteoblasts apparently become entangled in this newly formed tissue and form the *bone corpuscles*. The fetal cartilage is thus transformed into a spongy mass of primary osseous tissue whose spicules are formed by a core of calcified cartilage upon which are deposited successive layers of bony tissue with their included *lacunæ* and bone corpuscles.

Axial sections of long bones at this stage of ossification show all the above changes in regular succession from the fetal hyaline cartilage at the extremities to the primary bone with its marrow

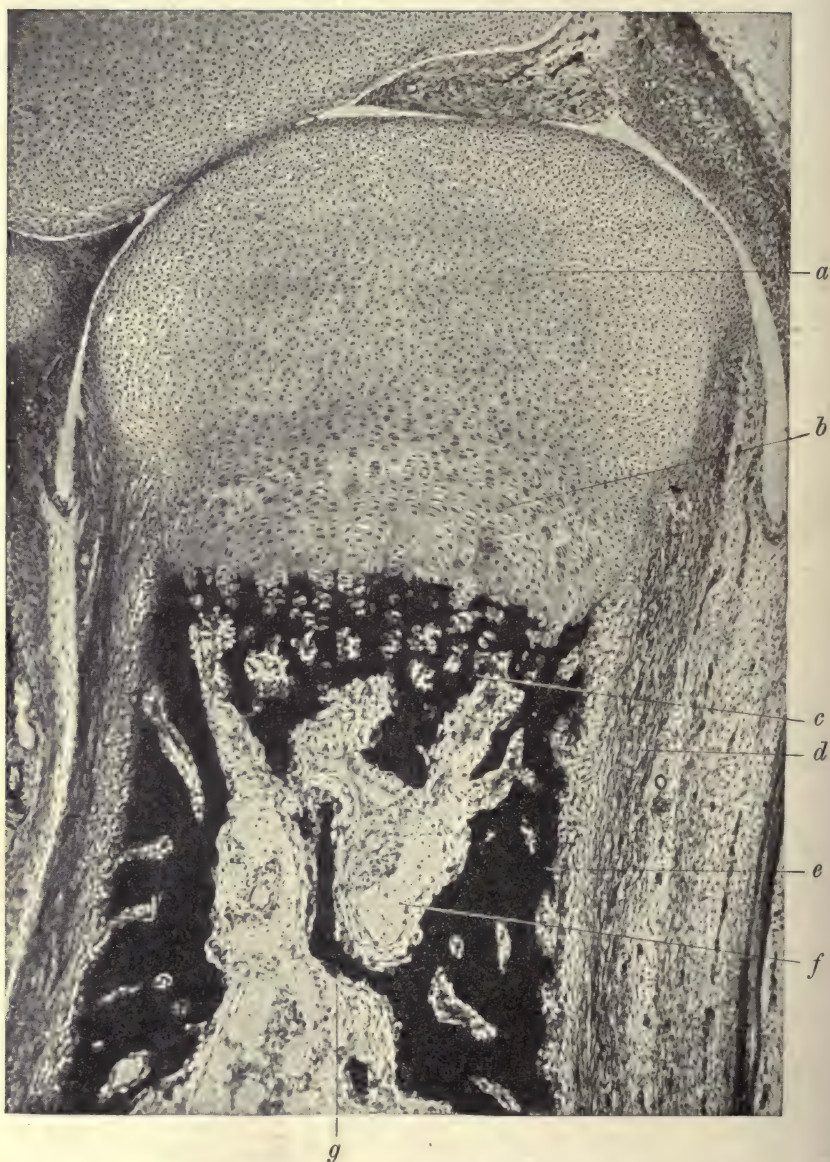


FIG. 167.—DEVELOPING BONE IN A PHALANX OF A FIVE MONTHS HUMAN FETUS.

a, Fetal cartilage; *b*, enlarged cartilage cells; *c*, primary bone; *d*, periosteum; *e*, periosteal bone; *f*, a thin-walled blood vessel within the marrow cavity; *g*, the line points to an osteoclast. Hematein and Congo red. Photo. $\times 69$.

cavities in the center. The process of ossification steadily progresses at the periphery, the line of enlarged cartilage cells constantly advancing farther and farther from the original center of ossification.

It is at this stage, however, that the giant cell *osteoclasts* become most active and the **absorption of the newly formed bone** progresses rapidly. The osteoclasts collect along the surface of the spicules of primary bone in considerable numbers and appear to sink into little recesses which they form within the bony tissue. The little bays which are thus formed in the primary bone are the *lacunæ of Howship*. The continued absorption soon breaks down and removes the trabeculæ and partitions of spongy bone and forms a central *medullary cavity* of constantly increasing size.

Coincident with these changes within the cartilage the osteogenic tissue which forms the inner layer of the periosteum produces successive layers of bony tissue upon the surface of the fetal cartilage. This process of **periosteal ossification** proceeds in a manner similar to that by which enchondral bone is formed. Osteoblasts arrange themselves upon the surface of the cartilage and deposit successive layers of bony tissue, between which many of these cells are included as bone corpuscles. At irregular intervals the osteoclasts collect and the primary periosteal bone is absorbed. Into these cavities buds of vascular osteogenic tissue push their way to form canals of considerable length. Upon the surface of the canals which are thus hollowed out of the periosteal bone, the osteoblasts deposit successive concentric layers of bony tissue and the *Haversian systems* make their appearance. Finally, upon the surface of the periosteal bone successive layers of newly formed bony tissue compose the *outer circumferential lamellæ*, while upon the wall of the medullary cavity a similar endosteal layer of bone-forming cells deposits the *inner circumferential lamellæ*.

With the formation of the periosteal bone the lateral expansion of the organ by enchondral bone formation necessarily ceases. Henceforth increase in diameter of the bone is only produced by continued absorption of the compact bony wall and the formation of new bone beneath the periosteum by frequent repetitions of the processes of periosteal ossification as already described. The remnants of those Haversian and circumferential lamellæ which are only partially absorbed in this process form the *interstitial lamellæ* of the mature bone.

During the processes of enchondral and periosteal ossification

within the shaft of the bone, the epiphysial cartilages continue to grow. Finally, however, ossification begins in the **epiphysis**, and,



FIG. 168.—TRANSECTION OF A RIB OF AN INFANT.
Developing bone. Hematein and eosin. Photo. $\times 67$.

proceeding in the same manner as in the shaft, results in the formation of primary spongy bone, some of which is absorbed and

replaced by more compact bony tissue, as occurs in the wall of the epiphysis. In its central portions the tissue retains its spongy arrangement and but few Haversian systems are formed. It is thus that the *cancellous bone* of this part, as also of the ends of the diaphysis, is formed.

At the point where the expanding centers of ossification of the shaft and epiphysis are about to meet, a line of unossified cartilage, the *epiphysial line*, persists until growth of the bone is complete. It is by growth of this cartilaginous disk, with continued formation of cartilage on its surface, that the bone increases its length.

The following is a *résumé* of the various stages of enchondral ossification :

1. Formation of the fetal cartilages.
2. Enlargement of the cartilage cells with a rearrangement into radiating cell rows at the center of ossification.
3. Absorption of the cartilage matrix and finally also of the cartilage cells. Appearance of calcified remnants of the cartilage matrix.
4. Eruption of the subperiosteal osteogenetic tissue and the formation of primary marrow cavities at the center of ossification.
5. Gradual extension of the above processes followed by a deposit of primary bone by the osteoblasts upon the calcified cartilage. Coincident osteoblastic deposit of periosteal bone beneath the perichondrium of the cartilage plate.
6. Absorption of portions of the primary bone by the osteoclasts to form the large central marrow cavity or medulla. The absorption involves both the enchondral and the periosteal bone and is accompanied by a further deposit of new bone at the periphery. In the periosteal bone cylindrical axial channels are formed, in which the deposit of new bone produces the Haversian systems of the compact bony tissue.

INTRAMEMBRANOUS OSSIFICATION.—In this type of bone formation, ossification occurs directly within the preconnective tissue of the mesoblast without the preliminary formation of cartilage. The earliest evidence of ossification consists in an enlargement of the mesenchymal cells which arrange themselves in the form of a membrane at the site of the future bone. Certain of these cells produce the periosteum ; others increase greatly in size, acquire a considerable cytoplasmic body, and assume the functions of the osteoblasts. The osteoblasts which are thus formed, not

only line the primitive periosteum but also form budding processes which project into the adjacent connective tissue.

Bone tissue is now formed by the *osteoblasts*. The deposit of the fibrous stroma precedes calcification and in this way brushes of radiating fibres frequently project from the osteogenic buds



FIG. 169.—INTRAMEMBRANOUS BONE FORMATION IN THE LOWER JAW OF AN EMBRYO SHEEP.

a, bone; *b*, primary marrow cavity; *c*, osteoblasts; *d*, growing point of the primitive bone, beyond which primary marrow is developing in the connective tissue of the mesoblast. $\times 300$. (After Böhm and von Davidoff.)

beyond the limit of the calcareous deposit. The bony processes thus formed are covered by a layer of osteoblasts which continue to deposit bony lamellæ, with their bone corpuscles and lacunæ, in the same manner as in enchondral bone formation: a mass of spongy bone results.

The *marrow* spaces of the cancellous bone are occupied by embryonic connective tissue in which are many small and thin-walled blood vessels. This primitive marrow differs from that of

the enchondral bone in the scarcity of its cellular elements ; otherwise the process of intramembranous bone formation is identical with that which forms the periosteal layers of the enchondral bone.

The after *absorption* of the bony spicules and partitions in intramembranous bone is very active, the osteoclasts appearing in considerable numbers. The contour of these bones is subject to frequent changes as a result of the continued absorption and new formation of bony tissue. The cancellous bone which is developed during these processes forms the mid-portion of the bone or diploë, the outer walls of the flat bone being formed by periosteal ossification as in the enchondral bones.

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CHAPTER XII

MUCOUS MEMBRANES—SECRETING GLANDS

THE histologic structures which are necessary for the formation of a secretion include an epithelial surface, and a tunica propria of connective tissue which supports the requisite blood and lymphatic vessels and the controlling nerve supply. These structures may either form smooth membranous surfaces or apparent epithelial invaginations. The former are found on the surface of the mucous membranes, the latter are the secreting glands.

MUCOUS MEMBRANES.—The mucous membranes may be said to include all those secreting surfaces which are directly or indirectly connected with the surface of the body, hence their epithelial clothing is continuous with that of the skin. The mucous membranes form the lining coat of the respiratory and alimentary systems, together with the ducts of their secreting glands: in the nose this membrane is continuous through the tear ducts with the conjunctiva of the eye and through the Eustachian tubes with the lining membrane of the middle ear. The broad expanse thus formed is known as the *gastro-pneumonic* mucous membrane. A second membranous sheet, the *genito-urinary* mucous membrane, clothes the organs of the genital and urinary systems: it thus forms the lining membrane of the vagina, uterus, and Fallopian tubes, of the urethra, bladder, and pelvis of the kidney, of the ducts and tubules of the prostate gland, the testis, and the smaller secreting glands which are connected with the genital system.

A mucous membrane consists of a superficial layer of epithelium of varying type, which rests upon a *basement membrane* (*membrana propria*) and is in turn supported by an investment of connective tissue, the *tunica propria*, or corium. The **tunica propria** is richly supplied with small blood vessels and lymphatics; its nerve fibrils are not only distributed to the walls of the blood vessels but in many cases send terminal filaments which enter the epithelial layer and terminate in contact with the secreting cells. The mucous membranes are mostly contained within hollow organs

which are subject to alternate collapse and distention; hence the membranes are frequently much folded. The deeper portion of the mucous membrane usually contains a more or less well-defined layer of smooth muscle fibres, the *muscularis mucosæ*.

The mucous membranes, as their name indicates, are nearly all moistened by a mucus containing secretion. The relative amount of mucus which its secretion contains, and consequently the viscosity of the secretion, bears a close physiologic relation to the intensity of the mechanical irritation to which the membrane is subjected. Thus the mucus secreting goblet cells of the gastro-pneumonic membrane are here and there reinforced by numerous mucus secreting glands of considerable size; these are especially abundant in the oral cavity, pharynx, and esophagus, and in the nose, trachea, and bronchi; in the urinary system even the goblet cells are absent.

The **basement membranes**, upon which the epithelium of the mucous membranes and the secreting glands is supported, are connective tissue structures. They are sometimes formed by interlacing bundles of delicate white fibres intermingled with numerous elastic fibres. Frequently, however, they consist of reticular tissue. Basement membranes of this nature have been demonstrated by Mall and his pupils in the mucous membranes and glandular tubules of the stomach, intestine, liver, salivary glands, kidney, testis, and thyroid. Occasionally basement membranes are homogeneous or hyaline in structure and present a more or less clear or glassy appearance.

SECRETING GLANDS.—The secreting glands may be quite properly considered as invaginations of the epithelial surfaces of the mucous membranes. They appear as such in the embryo. Their earliest anlage is formed by a solid or funnel-shaped process

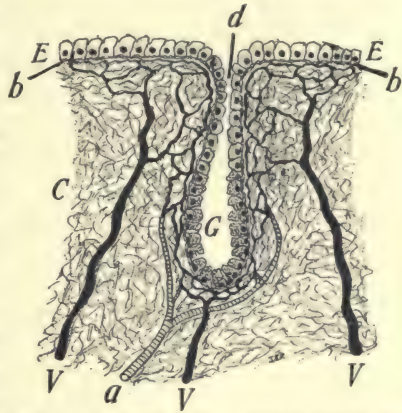


FIG. 170.—DIAGRAM OF A MUCOUS MEMBRANE HAVING SIMPLE TUBULAR GLANDS.

a, artery; *b-b*, basement membrane; *C*, connective tissue; *d*, duct of the gland, lined by cuboidal cells; *E*, epithelium of the free surface, clear, columnar cells; *G*, lumen of the fundus of the gland, lined by granular, serous secreting, columnar cells surrounded by secretory capillaries; *V*, veins. The arteries are striped, the capillaries and veins, black. Nerves are not represented.

of epithelium, in which a distinct lumen soon appears, and which grows into the surrounding mesoblast, carrying with it its embryonal tunica propria.

The form of the glandular invaginations is subject to great variation. They may be straight and simple, more or less branched and compound, convoluted or coiled, or the tubules may terminate in minute ampullary enlargements, the acini. The invaginations may also be distinctly tubular and of approximately equal diameter throughout, or they may form pouch-like saccules. According to the form of the organ, it is thus possible to distinguish the following

HISTOLOGIC TYPES OF SECRETING GLANDS:

- | | | |
|---------------------------------|---|----------------------------|
| | { | 1. Simple. |
| | | 2. Convoluted. |
| I. Tubular | | 3. Branched. |
| | | 4. Compound. |
| | | 5. Compound tubulo-acinar. |
| | { | 1. Simple. |
| II. Saccular | | 2. Branched. |
| | | 3. Compound. |
| III. Ductless secreting glands. | | |

Glands of the tubular and saccular types contain an actively secreting portion or *fundus* and a *duct*. In the ductless glands the latter is absent. The duct, though its epithelium may take some part in the formation of the glandular secretion, primarily serves to convey the secretion of the fundus to the free surface of the mucous membrane.

The epithelium of the duct, as a rule, more or less closely resembles that of the mucous membrane upon whose surface it opens. The epithelium of the fundus, on the other hand, usually differs from that of the duct and varies according to the nature of its secretion. In many of the glands the epithelium is typically *mucus* secreting; others produce a clearer, watery, and less viscid *serous* secretion. Hence it is possible to distinguish the following

PHYSIOLOGIC TYPES OF SECRETING GLANDS:

- I. Serous glands.
- II. Mucous glands.
- III. Glands which are both mucous and serous (mixed glands).
- IV. Glands which are neither mucous nor serous.

This physiologic classification is not in any way the equivalent of the histologic gland types mentioned above. Thus both serous and mucous glands, in different locations, form almost every variety of tubular gland.

The glands of the fourth type are too varied in their structure to be considered collectively to advantage. The reader is referred to the several chapters in which they are described in detail. This type includes the testis, the prostate, the ceruminous glands, many of the ductless glands, and also some authors describe the ovary and the lungs as conforming to the glandular type of structure.

The mixed secreting glands include some tubules which are characteristically mucous, while others are typical serous secreting. Occasionally both types of secreting cells are contained within the same tubule.

Mucous secreting cells possess the general characteristics which have been previously recited under the head of goblet cells (Chapter II). When void of secretion the cytoplasm of mucous cells is granular, their nucleus centrally situated, and their shape more or less columnar. The pre-secretion accumulates in the central portion of the cell and occupies an area, adjacent to the glandular lumen, which steadily increases in size until the greater part of the cytoplasm has been replaced; the nucleus is pushed to the distal or attached end of the cell; and the whole cell often becomes swollen and distended to more than double its original size. Finally the cell membrane ruptures and the mucus pours out upon the free surface of the membrane.

At the base of the mucous secreting cells, and between them and their basement membrane, are groups of epithelial cells having a finely granular cytoplasm, which form crescentic cell masses, the *demilunes* of Heiden-

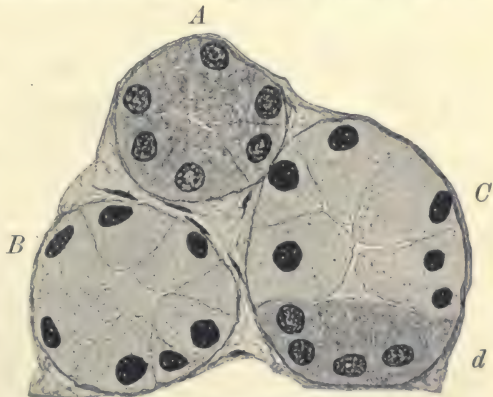


FIG. 171.—TRANSECTION OF THREE SECRETING TUBULES OF THE SUBMAXILLARY GLAND OF MAN.

A, a serous tubule; B, a mucous tubule; C, a mucous tubule with a demilune, d. Hematein and eosin. $\times 665$.

hain (crescents of Gianuzzi). In the tubules of some glands these demilunes are extremely minute, in others they occupy a considerable portion of the epithelial coat and encroach upon the glandular lumen. Their significance is not definitely understood. They have been considered as representing either secreting cells which are in a state of rest following the discharge of their secretion, or as primordial cells which by reproduction give origin to true mucous secreting cells. It is quite possible that both of these functions are assumed by the several cells which compose the demilunes.

Mucus, the product of the mucous secreting cells, possesses peculiar properties. In the fresh condition it has a clear, glairy appearance and a pearly white color. Acted upon by alcohol or acids it gives a heavy precipitate of stringy white flocculi. Within the tissues these delicate flocculi stain slightly with basic dyes and readily with the muchematin and mucicarmin of Mayer. The very clear glairy appearance of the fluid and the slightly basophile properties of the precipitated flocculi are so characteristic that when typical mucus containing cells are once carefully observed they can be thereafter most readily distinguished from other types of epithelium.

Serous secreting cells differ greatly in appearance with the varying character of their secretions, yet they present certain general characteristics. These cells are unquestionably capable of alternate phases of secretory activity and comparative rest. At the end of a period of activity they appear shrunken and small, and the lumen of their tubule is consequently increased in size. Their nucleus is centrally located, and their cytoplasm is relatively devoid of secretion and frequently presents a faintly rodlike or striated appearance.

During *rest* secretion accumulates within the cell, and the cytoplasm consequently becomes either clearer or more granular, according as the nature of the secretion is watery, or is granular and zymotic in character; thus the secreting cells of the sweat glands become clearer as their secretion accumulates, whereas those of the pancreas become more granular.

As a rule the pre-secretion accumulates at the central end of the cell, the nucleus is thus crowded toward the basement membrane and is surrounded by the least altered cytoplasm. The whole cell becomes swollen and distended by the accumulated secretion and the tubular lumen is consequently diminished in size or even occluded.

Finally the period of *secretory activity* arrives, and the secretion is poured into the glandular lumen; the cells become shrunken and the lumen of the tubule correspondingly dilated. The cytoplasm returns to its former condition; if the secretion is of a granular character the cell becomes clearer, but if watery the cytoplasm acquires a finely granular appearance. The nucleus resumes its former central location and the cell enters upon a second period of constructive and accumulative activity.

Many of the serous secreting cells contain minute *intracellular canals* which connect with a network of *intercellular passages* about the cell. The intercellular canaliculi may, on the one hand, open into the glandular lumen, or they may communicate with the tissue spaces of the tunica propria. This system of intracellular and intercellular canaliculi may thus serve either as a system of nutrient channels or as a network of secretory capillaries by which the secretion is conveyed from the interior of the secreting cells to the lumen of the gland or even to the duct system. Nutrient and secretory canaliculi of this nature have been demonstrated in the secreting cells of the liver, cardiac glands of the stomach, salivary glands, pancreas, adrenal, and epididymis, but they are not by any means confined to the actively secreting cells, for they have been found in the cells of bladder epithelium (Holmgren) and are highly developed in the nerve cells (Holmgren, Golgi, *et als.*).

Simple tubular glands occur in the mucous membrane of the small and large intestine as the crypts of Lieberkühn. In shape these glands resemble a test-tube. They form straight tubules which open on the free surface of the membrane, are of approximately equal caliber throughout, and at their deeper end terminate in a blind extremity. The tubules are lined with epithelium and are embedded in a thin vascular tunica propria. Their epithelium includes the usual columnar and goblet cell types, the latter being more abundant near the mouth of the gland. Near the blind extremity are certain granular cells, the granules of some of which are slightly basophilic: other cells possess coarse granules which are highly acidophile, as demonstrated by Kultschitsky* in the intestinal glands of the dog, an observation which is easily corroborated for the simple tubular glands in the small intestine of man.

* Arch. f. mik. Anat., 1897.

Convoluted tubular glands occur as the sweat glands of the skin, the ceruminous glands of the ear, and the glands of Moll in the eyelids. The above are typical simple coiled glands. Certain

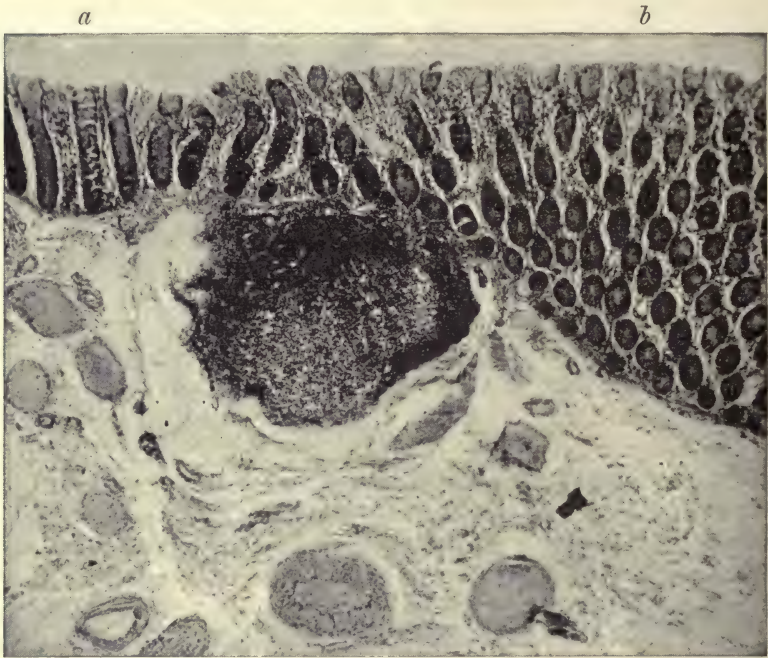


FIG. 172.—FROM THE LARGE INTESTINE OF MAN.

Showing simple tubular glands in longitudinal section at *a*, and in transverse and oblique section at *b*. Hematein and eosin. Photo. $\times 48$.

other glands, which are less typically coiled but are more or less convoluted near their blind extremities and are frequently branched, are also to be included under this type. Such glands are the pyloric glands of the stomach, and the small mucous glands of the oral and nasal cavities, pharynx, larynx, trachea, bronchi, and esophagus. Some of these glands, and especially those of the pyloric end of the stomach, present terminal acinar dilata-tions, hence they also resemble to some extent a small tubulo-acinar type of gland.

The typical *coil glands* consist of a duct whose epithelium resembles an attenuated layer of the stratified epithelium upon which they open, and a fundus or secreting portion which is lined by columnar epithelium of the glandular type. They also possess

a connective tissue basement membrane and a vascular tunica propria.

Branched tubular glands include the cardiac or fundus glands of the stomach and the glands of the uterine mucous membrane. These glands possess a duct whose epithelium corresponds in type with that of the surface upon which they open. Several secreting tubules open into this duct by means of a short constricted por-

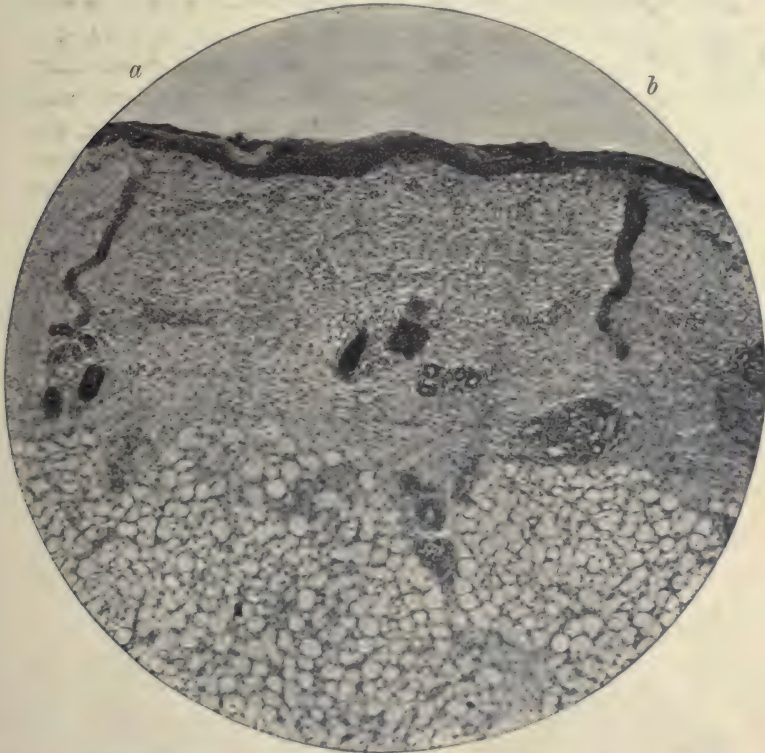


FIG. 173.—CONVOLUTED TUBULAR GLANDS (COIL GLANDS) IN THE SKIN OF AN INFANT.

The duct of the gland directly beneath *a* does not quite reach the epithelial surface in the plane of this section; in that beneath *b* the duct is separated from the secreting portion. Hematein and eosin. Photo. $\times 65$.

tion, *the neck*. The fundus or secreting portion, after a typically spiral course, ends with a blind extremity which is often curved or hooked. This portion of the gland is clothed with columnar or glandular epithelium and invested with a thin basement membrane and tunica propria.

Compound tubular glands include the kidney, testis, lachrymal gland, and liver. The finer structure of the glands of this type is so peculiar that the reader must be referred to the several chapters in which they are more fully described.

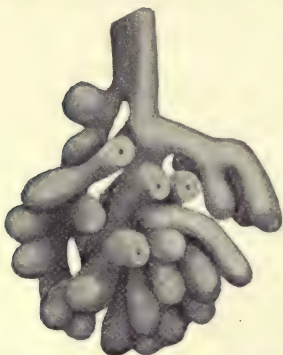


FIG. 174.—MODEL OF A RECONSTRUCTION OF THE LACHRYMAL GLAND OF MAN.

The tubular duct divides into the terminal secreting tubules. $\times 170$. (After Maziarski.)

a much branched tree, whose stem as the main *excretory duct* opens upon



FIG. 175.—RECONSTRUCTION OF A MUCOUS GLAND FROM THE RESPIRATORY REGION OF THE NASAL MUCOSA OF A CHILD.

The duct passes directly into the secreting alveoli. A typical small tubulo-alveolar gland. $\times 200$. (After Maziarski.)

Compound Tubulo-alveolar Glands (*Tubulo-acinar or Racemose Glands*).—

This is the most widely distributed of all the types of secreting glands. It includes the parotid, the submaxillary, the larger mucous and serous glands of the oral cavity, and of the nose, pharynx, trachea, bronchi, and esophagus, Brunner's glands in the duodenum, the pancreas, Cowper's glands, Littre's glands, and the large mucous glands of the cervix uteri.

The form of these glands may be likened to



FIG. 176.—RECONSTRUCTION OF AN INTRA-LOBULAR DUCT DIVIDING INTO ITS TERMINAL INTERCALLARY DUCTS AND ACINI.

The terminal divisions of a large compound tubulo-acinar gland. The model was made from serial sections of the human pancreas. $\times 344$. (After Maziarski.)

the free surface of a mucous membrane, and the branches and twigs as the larger and smaller interlobular ducts reach out in all directions to finally end in minute alveolar dilatations, the secreting *acini*.

Except for the ducts of certain mucous glands whose epithelial coat resembles that of the mucous membrane to which they are attached, the ducts of this type of secreting gland are lined by columnar cells whose cytoplasm frequently presents a rodlike appearance at the deeper end of the cell. The acini contain typical serous or mucous, secreting epithelium. Occasionally the secreting cells are also found for some distance beyond the acinus in the lining membrane of the smallest ducts.

The tubules and acini of these glands are invested with a basement membrane and a delicate tunica propria. The acini are united by the connective tissue into small groups which inclose a central duct of the smallest type, the *intercalary duct*. These acinar groups are again united into the *lobules* of the gland by fine bands of connective tissue, and broader bands of loose connective tissue cement the many lobules into one glandular mass. The intercalary ducts by union within the lobule form numerous small *intralobular ducts* which approach the periphery of the lobule and at its margin open into the *interlobular ducts*; the latter are found in the broader septa of connective tissue between the lobules. The interlobular ducts by union with one another result in progressively larger branches which finally form the main *excretory duct* of the gland.

Simple saccular glands occur as the smallest sebaceous glands of the skin. These are small glandular pouches with a short duct, a constricted neck, and a dilated fundus which, instead of having a single coat of epithelium as in most of the tubular glands, is more or less completely filled with a mass of epithelial cells. The cells as they approach the duct of the gland show progressive stages of degeneration and disintegration which culminate in the formation of a thick, viscid, fatty secretion. Since these cells form their secretion by disintegration they are obviously capable of passing through the various stages of secretory activity but once, and hence they must be renewed by the repeated mitotic cell division which occurs at the periphery of the saccule.

The epithelium of the secreting saccule rests upon a distinct basement membrane and is invested with a very vascular tunica propria.

Branched saccular glands include the larger of the sebaceous glands of the skin, in which several saccules pour their secretion into a common duct, and the Meibomian glands of the eyelids in

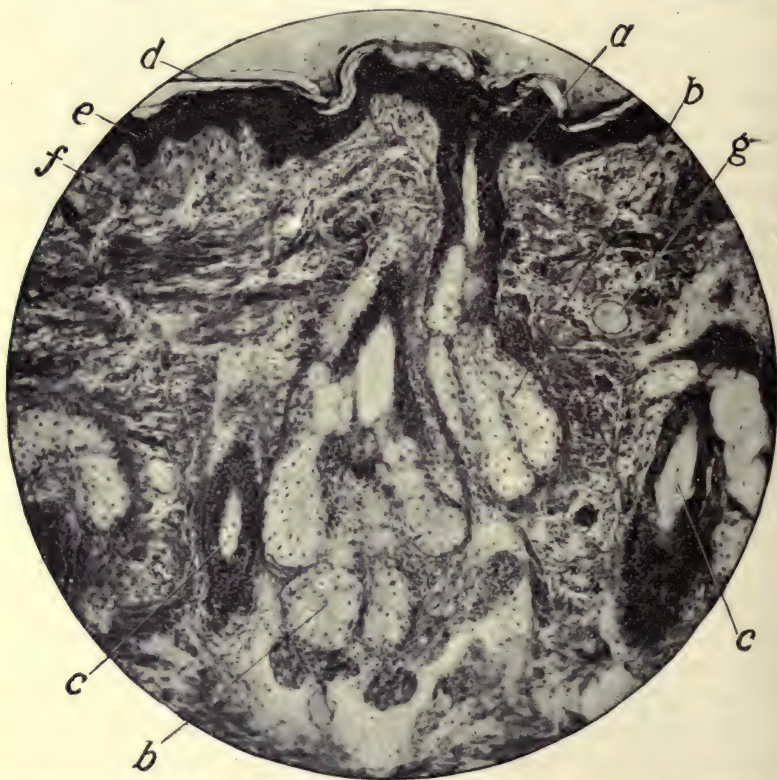


FIG. 177.—FROM THE SKIN OF A CHILD, SHOWING BRANCHED, SACCULAR, SEBACEOUS GLANDS.

a, hair follicle into which the duct of a gland opens; *b*, secreting saccules; *c*, hair follicles; *d*, horny portion of the cutaneous epithelium; *e*, germinal portion of same; *f*, connective tissue of the skin; *g*, blood vessel. Hematein and eosin. Photo. $\times 83$.

which a considerable number of saccules open into an axial canal by which the secretion is conveyed to the terminal duct. The structure of each glandular saccule of this type is identical with that of a simple saccular gland.

Compound Saccular Glands.—This type includes only the mammary gland. It consists of a system of tubular ducts which possess ampullary dilatations and many branches. Its ducts terminate in small saccular alveoli which have a thin epithelial lining.

During the period of their inactivity the lining epithelial cells are much flattened and the acini appear shrunken. The epithelium of the lactating gland, on the other hand, is cuboidal or columnar, the height being more or less dependent upon the accumulation of secretion within the cell.

The secretion is formed in the same manner as in the tubular glands with an additional process of fatty infiltration by which fat droplets are formed within the cytoplasm. These droplets collect in the central portion of the cell and are finally discharged into the lumen of the acinus with apparent rupture of the cell membrane and the escape of a portion of its superficial cytoplasm. The epithelium is thus capable of repeated secretion.

The mammary glands may be considered as offering an intermediate type between the branched saccular and the tubulo-acinar types.

Ductless Glands.—Under the head of secreting glands it is necessary to consider certain structures which apparently contain secreting epithelium and which present a more or less distinct tubular arrangement. These bodies are the adrenals, thyroids, parathyroids, carotid glands, coccygeal gland, and hypophysis cerebri.

While these bodies do not possess an excretory duct, nevertheless some of them certainly, and the others probably, form certain products which find their way into the blood or lymph as so-called "*internal secretions*." The epithelium of the glands may form either alveoli, tubules, or solid cell columns, which are supported by very delicate connective tissue tunics. Many blood vessels, often of the thin walled sinusoidal type, are found within these tunics and are thus brought into intimate relation with the epithelial parenchyma. In some instances lymphatics are distributed in a similar manner within the gland.

The property of internal secretion is not peculiar to the ductless glands. It has long been ascribed to the liver cells in connection with their influence upon nitrogenous and carbohydrate metabolism, and, in fact, many secreting glands, even though not of vital importance, are nevertheless found to influence the economy in certain ways which can not be accounted for by the properties of their external secretions.

Finally, it must be emphatically stated that the types of secreting glands, as above described, are not bound by hard and fast

lines, but many forms will be found which might well be placed under either of two or more types. Hence any classification of secreting glands becomes more or less arbitrary; nevertheless such a classification is of extreme importance as serving to establish in the mind of the student certain typical pictures with which individual glands may be compared, and important structural details will thus be noticed which might otherwise escape observation.

CHAPTER XIII

THE SKIN

THE skin contains a layer of dense connective tissue, the corium or derma (derma vera, cutis vera), which corresponds to the tunica propria of the mucous membranes, and is everywhere covered by a layer of stratified squamous epithelium, the epidermis (cuticle). The corium contains the nerves and the nerve end organs of special sense, and rests upon a subcutaneous layer of areolar and adipose connective tissue which firmly unites the skin to the underlying organs and tissues.

The skin is typically a stratified organ, and for convenience of description may be divided into the following layers:

SKIN.	{	I. Epidermis.	{	1. Scaly layer.	{	Horny layer.
		{		2. Flattened cell layer.		
				3. Eleidin containing layer.		
	{	II. Derma.	{	4. Granular layer.	{	Malpighian or "mucous" layer.
				5. Prickle cell layer.		
				6. Cylindrical cell layer.		
		III. Subcutaneous tissue.				

THE EPIDERMIS

The epidermis (cuticle) serves for the protection of the more sensitive corium or "true skin." It is formed by a dense layer of stratified epithelium and varies in thickness in different portions of the body, being thickest upon those surfaces which are exposed to the greatest mechanical violence, e. g., the palms of the hands and soles of the feet; and thinnest in the least exposed portions, e. g., inner sides of the arms and the back.

The layer of stratified epithelium composing the epidermis differs from that of the mucous membranes in that its superficial cells contain an abundance of keratin, a peculiar horny material. The production of keratin in the cells of stratified epithelium appears to be more or less dependent upon the desiccation which occurs in those cells which form the comparatively dry cutaneous surface. The cornification can scarcely be demonstrated in the stratified squamous epithelium of the moistened mucous membrane of the mouth, esophagus, etc. ; it is present though not pronounced in the partially moistened margins of the eyelids, lips, labia minora, glans penis, etc. In the epidermis, however, cornification is pronounced and characteristic in all portions of the body.

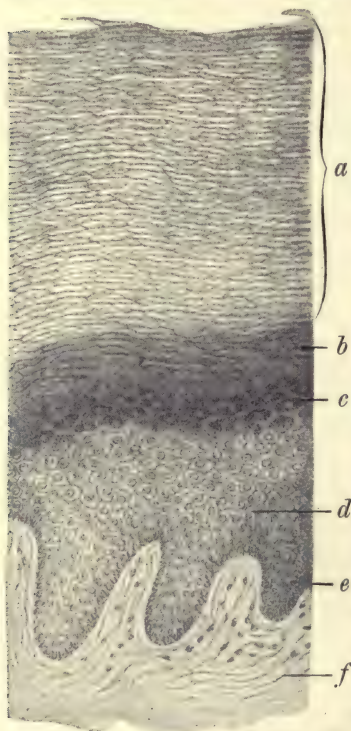


FIG. 178.—EPIDERMIS OF THE FOOT.

a, flattened cells; *b*, stratum lucidum; *c*, granular layer; *d*, germinal layer; *e*, cylindrical cell layer; *f*, derma. Picro-carmin. Moderately magnified. (After Ranvier.)

The thickness of the cornified layers appears to be in proportion to, if not entirely dependent upon, the amount of mechanical violence to which the cutaneous surface is subjected. Accordingly the increased thickness of the epidermis covering the palms and soles is found to be due almost entirely to an increase in the superficial horny portion of the epidermis, the germinal layers being no more pronounced than in other portions of the body.

The epidermal tissue is divisible into a superficial horny portion consisting of flattened, desiccated, cornified cells—the stratum corneum or horny layer—and a deeper protoplasmic, so-called “mucous” portion, which consists of polyhedral and cylindrical cells—stratum mucosum, rete mucosum, rete Malpighii.

Cylindrical Cell Layer (*Stratum Cylindricum*).—The deepest cells of the stratum mucosum are elongated in a direction nearly perpendicular to the basement membrane upon which they rest;

they are thus irregularly cylindrical in shape. It is these cells which in the pigmented portions of the body, i. e., areolæ of the nipples, scrotum, circumanal region, etc., and in the skin of brunettes and the colored races contain the pigment which gives rise to the darkened color of the skin. The processes of mitotic cell division are very active in these columnar cells, and they, with the adjacent portion of the prickle cell layer, form the *stratum germinativum* of Fleming, in which the regeneration of the epidermis occurs. The cylindrical cells are firmly united to the basement membrane by delicate cytoplasmic fibrils, the intercellular bridges. Their nuclei are ovoid in shape, and vesicular in appearance.

Prickle Cell Layer (*Stratum Spinosum*, *Stratum Filamentosum* of *Ranvier*).—Superficial to the cylindrical cells is a stratum of polyhedral epithelium which extends inward between the adjacent papillæ of the corium (*interpapillary region* of the epidermis), and is therefore thick in these portions, but is relatively much thinner over the apices of the dermal papillæ (*suprapapillary portion* of the epidermis).

The polyhedral cells of this layer contain a soft granular cytoplasm and a very chromatic, though vesicular, spheroidal nucleus. They are separated from one another by narrow intercellular spaces which are bridged across by innumerable delicate cytoplasmic fibrils. These fibrils connect adjacent cells and are frequently continued without interruption through one, two, or even three or four neighboring cells. Their course is characteristically curved, the convexity being directed toward the nucleus. Those portions of the numerous cytoplasmic fibrillæ which span the intercellular spaces form the so-called *intercellular bridges*. It is because of the resulting spinous appearance that the polyhedral cells have been termed *prickle cells* (Schultze).

In the thinner portions of the epidermis the prickle cells are immediately covered by several layers of hard flattened cells whose nuclei have partially or wholly disappeared, and whose cytoplasm has been changed into a horny, keratin containing mass. The flattening and desiccation of these cells becomes more pronounced as they approach the surface. In the thin portions of the epidermis the change from the prickle cell layer to the horny layer is abrupt.

In the thicker portions of the epidermis, as in the palms of the hands, the change is more gradual, and results in the appearance of two additional cell layers, in the cytoplasm of whose cells are

intermediate products of chemical metamorphosis, keratohyalin and eleidin, which may be considered as the predecessors of the keratin which is peculiar to the cells of the horny portion.

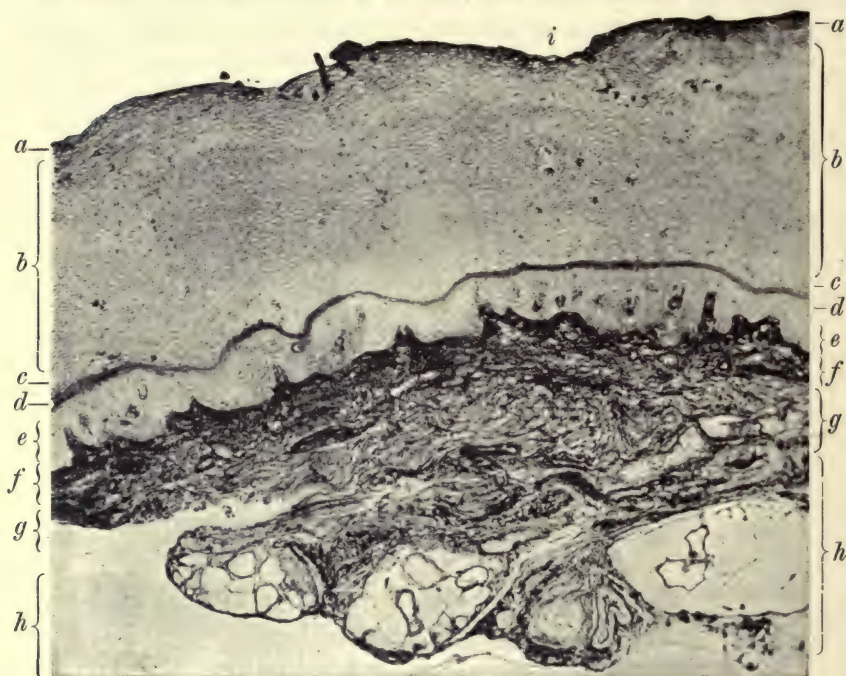


FIG. 179.—TRANSECTION OF THE SKIN OF A HUMAN FINGER.

a, scaly layer; *b*, layer of flattened cells; *c*, stratum lucidum, appearing indistinct in this preparation; *d*, granular layer; *e*, germinal layer; *f*, papillary layer of the derma; *g*, reticular layer; *h*, subcutaneous connective tissue; beneath *i*, the duct of a sweat gland is seen in the middle of the epidermis. Hematein, Weigert's elastic tissue stain, and picro-fuchsin. Photo. $\times 48$.

Granular Layer (*Stratum Granulosum*).—In the thicker parts of the cuticle the most superficial prickles cells become slightly flattened, and coarse granules appear within their cytoplasm. These cells form the granular layer (*stratum granulosum*), a double cell layer which occupies the superficial portion of the rete mucosum.

The cells of the granular layer are flattened and angular. They possess an indistinct, apparently degenerating nucleus, and their cytoplasm contains large plate-like granules of *keratohyalin* (*eleidin* of Ranvier), which are strongly basophile and stain readily with most nuclear dyes.

Eleidin containing Layer (*Stratum Lucidum*).—The granule cells are abruptly transformed into the shiny cells of the stratum lucidum, which is the deepest layer of the horny portion of the epidermis. The cells of this layer possess an indistinct nucleus, are irregularly flattened and angular in shape, are more or less fused together at their adjacent margins, and contain a smooth, highly refractive, glassy cytoplasm which reacts feebly to most staining reagents, but is deeply colored by safranin.

The stratum lucidum is so named because of its highly refractive appearance; it is usually about two cells thick. Its cytoplasm contains *eleidin*, a substance which is probably intermediate in chemical composition between the keratohyalin of the stratum granulosum and the keratin of the horny cells.

Flattened Cell Layer and Scaly Layer (*Stratum Corneum* and *Stratum Disjunctum* of Ranvier).—Above the stratum lucidum the horny layer consists of flattened cornified cells which are closely packed and somewhat fused and blended with each other at their faintly serrated margins. Intercellular bridges and spaces have almost entirely disappeared. The nuclei of the cells are no longer demonstrable, and their cytoplasm has been changed into a dry, shiny, highly refractive mass of *keratin* which responds but slightly to ordinary stains. If, however, these cells are acted upon by solutions of strong alkalies, soda, potassa, etc., the outlines of the degenerated nuclei reappear. As the cells are pushed nearer the free surface, by the process of cell division in the deeper layers and the coincident desquamation of cells from the free surface, they become more and more flattened and desiccated and more completely and firmly fused together until at the surface they form the partially detached cell masses or scales—scaly layer, stratum squamosum—which are eventually removed by continued desquamation.

As Ranvier* has shown, sections of the epidermis which have been fixed in osmium tetroxid solutions are peculiarly blackened by this reagent. The horny layer only, reacts to the osmium, its superficial scaly layer as well as the deepest portion of the flattened cell layer being blackened by the reagent. The intervening portion of the horny layer is not stained with osmium except at the free margins of the tissue. Hence this reaction would seem to demonstrate the presence of a fatty material (*epidermal fat*)

* *Traité technique d'histologie*; also *Arch. d'anat. mic.*, 1900.

within the cells of the horny layer, which is apparently the result of certain of those degenerative changes which characterize this portion of the epidermis.

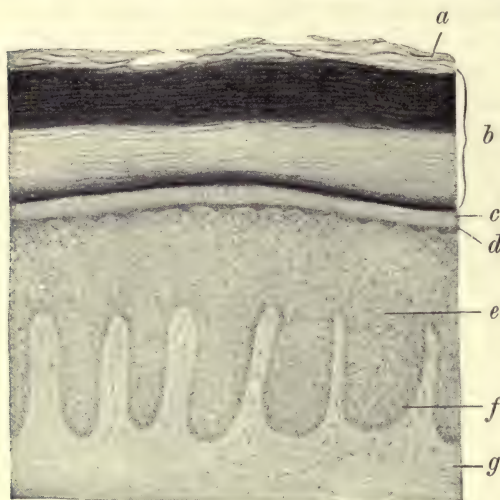


FIG. 180.—TRANSECTION OF THE EPIDERMIS OF THE FOOT.

a, superficial scaly layer; *b*, layer of flattened cells, the inner and outer portions of which have been characteristically blackened by osmium tetroxid; *c*, stratum lucidum; *d*, granular layer; *e*, prickle cells; *f*, cylindrical cells; *g*, papillary layer of the derma. Osmium tetroxid, carmin. Moderately magnified. (After Ranvier.)

The peculiar absence of the osmic reaction in the mid-portion of the horny layer can only be explained by the supposition that the osmium solution is unable to penetrate the dense horny layer except for a short distance from the free surface, from the free margins of the tissue, and from the more easily penetrated rete mucosum. The presence of the fatty material in the deeper part of the horny layer is not in accord with the idea that it is derived from the secretion of the

various cutaneous glands, i. e., the sudoriparous and sebaceous glands.

It is the thicker portions of the epidermis only, which possess all the characteristic layers above described. In other portions of the body the horny layer is much thinner (Fig. 181). In these thinner parts the cuticle of the epidermis consists of a prominent rete mucosum which is covered by a relatively very thin layer of horny cells. The stratum granulosum, in such portions, is not usually demonstrable, the stratum lucidum is absent or indistinct, and the entire horny layer consists only of flattened cornified cells, the more superficial of which form a very thin scaly layer.

THE DERMA

The derma or *corium* (derma vera, *cutis vera*) forms a connective tissue bed or matrix upon which the epidermis lies. It is

divisible into two strata, a deeper reticular layer in which coarse fibre bundles interlace to form a loose connective tissue network, and a superficial papillary layer in which the finer bundles of connective tissue form a more closely meshed network.

The Papillary Layer.—The surface of the papillary layer presents numerous conical elevations, the *papillæ* of the corium, which project into corresponding cup-shaped cavities in the under surface of the epidermis. Many of the connective tissue papillæ contain tactile end organs (touch corpuscles of Meissner), and terminal filaments of the nerve fibres. They may therefore be regarded as the special organ of tactile sensation. Other papillæ contain no touch corpuscles but are richly supplied with capillary blood vessels. Two types are thus distinguished, the *tactile papillæ* and the *vascular papillæ*.

Papillæ are most abundant in the palms of the hands and the soles of the feet, where they are mostly arranged in rows which are responsible for the fine lines and ridges visible to the naked eye. In other portions of the body they are less numerous and are often less regularly disposed.

The papillary layer consists entirely of white fibrous and elastic connective tissues which form a supporting membrane for the finer branches of the cutaneous blood vessels and nerves. The elastic tissue supplies a rich network of fine fibrils to all portions of the papillary layer, and just beneath the epidermis it forms a delicate elastic membrane whose fibres intermingle with the hyaline cuticular deposit of the columnar epidermal cells to form a firm resistant *basement membrane*. Many of the elastic fibres of the papillæ, especially the more superficial ones, pursue a peculiar archiform course from the base to the apex of the conical papillæ. In this way they surround and inclose the centrally situated capillaries and the tactile corpuscles of the papillæ.

The Reticular Layer.—The deeper portion of the corium consists of interlacing bundles of connective tissue fibres which form a dense reticulum. These bundles are much coarser than those of the papillary layer with which they are imperceptibly blended. The reticular layer contains the larger blood vessels of the corium, many small nerve trunks, the ducts and parts of the secreting portions of the sweat glands, the more superficial sebaceous glands, and many of the smaller hair follicles. Pacinian corpuscles and nerve end organs of Ruffini are also found in this layer.

The skin of the face contains many striated muscle fibres

which are derived from the insertions of the mimetic muscles. The corium of the scrotum (where it forms the tunica dartos), of the penis, perineum, and areola of the nipple contain much smooth muscle.

SUBCUTANEOUS TISSUE

The subcutaneous tissue (*tela subcutanea*, *panniculus adiposus*, *subcutis*) consists of bands and septa of fibrous connective tissue which extend from the deeper margin of the derma to the underlying fasciæ of the muscles, the periosteum of the bones, etc. The direction of these fibrous bundles is very variable. The more nearly parallel to the cutaneous surface the fibre bundles are, and the looser the meshes which they form, the greater is the mobility of the skin.

The meshes of the subcutaneous network are occupied by *lobules* of adipose tissue. The subcutaneous tissue contains the main nerve trunks and larger blood vessels of the skin, the larger sudoriparous and sebaceous glands, and the coarser hair follicles. It also, together with the deeper part of the derma, contains the nerve end organs of Pacini, Ruffini, and the Golgi-Mazzoni corpuscles.*

Small bundles of smooth muscle fibres which form the arrector pili muscles take origin from the deeper surface of the corium and are inserted into that portion of the hair follicle which is embedded in the subcutaneous tissue. These fusiform or columnar muscle bundles are found in connection with all the hairs, but in the scalp they are most highly developed and lie most deeply in the subcutaneous tissue.

DEVELOPMENT AND GROWTH OF THE SKIN.—The skin may be said to arise with the first differentiation of the embryo into its three germinal layers. The ectoblast, which is at first a single cell layer, becomes a double layer by the end of the first month. It continues to increase in thickness until by the end of the second month it can be differentiated into two layers, a superficial or *epitrichium*, and a deeper *germinal layer*.

The *epitrichium* forms a layer of peculiar dome-shaped cells with flattened margins and a vesicular center. It continues to form the superficial layer of the epidermis until about the sixth month, when it is lost by desquamation. The germinal layer consists of a deep stratum of cylindrical cells and one or two superfi-

* See Chapter IX.

cial strata of spheroidal vesicular cells. The latter are known as the *stratum intermedium*. By the fifth or sixth month cell differentiation has advanced in the intermediate portion until cornification can be distinguished in its superficial cells.

Further development is analogous to the growth of the mature epidermis; new cells are rapidly formed in the deeper portion, stratum germinativum, and are steadily pushed toward the surface, their migration being either accompanied by slight, or later by more pronounced cornification, which in the latter case gives rise to the stratum granulosum, stratum lucidum, and horny layer, but in the former produces only relatively slight flattening of the superficial cells without the appearance of keratin or the disappearance of the nucleus.

The derma arises from the superficial layers of the mesoblast as ordinary connective tissue, in which the appendages of the skin make their appearance as ingrowths from the epidermis. Certain mesenchymal cells form the smooth muscle fibres of the arrector pili muscles and of the derma of those locations where muscle is present in the mature skin. Other mesenchymal cells produce the fat lobules of the subcutaneous tissue. Papillæ appear during the fourth or fifth month but do not attain their completed development until much later.

The **CUTANEOUS APPENDAGES** include the sudoriparous glands, the nails, the hairs, and the sebaceous glands.

SUDORIPAROUS GLANDS (*the Coil Glands, Sweat Glands*).—

The sudoriparous glands occur in all portions of the skin, but more abundantly in certain locations, e. g., palms of the hands, soles of the feet, axillæ, groin, and circumanal region. They are long, coiled or convoluted, tubular glands whose secreting portions lie in the subcutaneous tissue and in the deeper part of the corium; their ducts extend through the corium to the under surface of the epidermis where the lining epithelium of the duct becomes continuous with the cells of the interpapillary portion of the stratum germinativum. In its further course through the epidermis the duct of the gland forms only a tortuous spiral cleft or passage whose wall is formed only by the concentrically placed cells of the various epidermal layers through which it passes.

The secreting or coiled portion of the gland (fundus) consists of a delicate hyaline membrana propria in whose outer portion are concentrically disposed connective tissue fibres. The inner por-

tion of this membrane contains many longitudinal fusiform fibres whose nature is somewhat doubtful, though they have been most frequently considered to be smooth muscle fibres.* These fibres

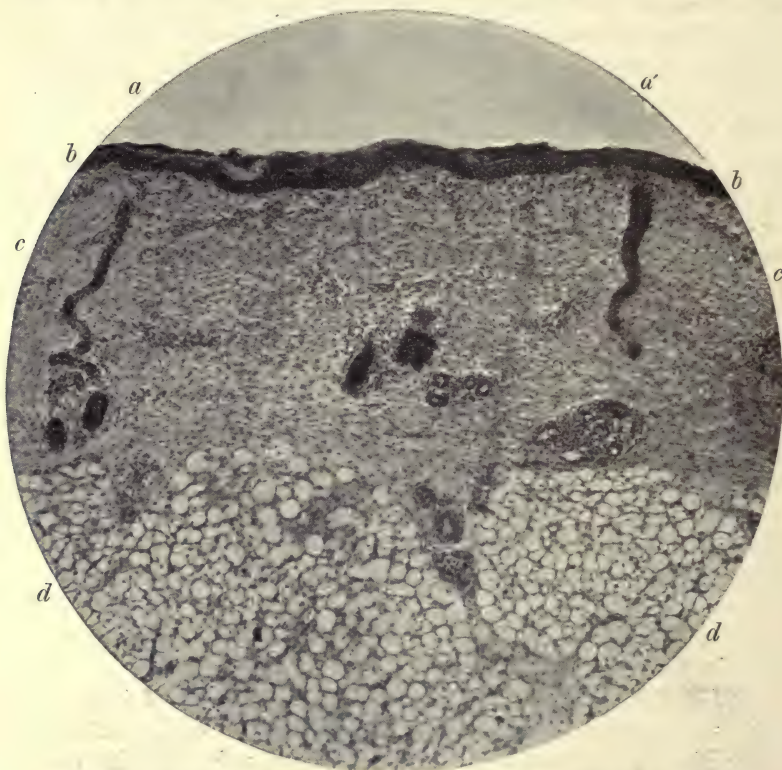


FIG. 181.—FROM A SECTION OF THE ABDOMINAL INTEGUMENT OF AN INFANT.

Beneath *a*, and *a'*, sweat glands are seen; the secreting portion at *a'* is detached from its duct; *b*, *b'*, epidermis; *c*, *c'*, derma; *d*, *d'*, panniculus adiposus. Hematein and eosin. Photo. $\times 65$.

are frequently branched, their processes often extending between the cells of the secreting epithelium nearly to the lumen of the gland.

The secreting epithelium of the fundus consists of tall columnar cells which possess a large spheroidal chromatic nucleus and

* The recent observations of Mallory (J. Med. Research, 1903) indicate that these fibres are a peculiar type of connective tissue element which he names *fibroglia*. Similar though smaller fibres are found in the basement membranes of other tubular glands—e. g., kidney, lachrymal, and mammary glands.

a finely granular cytoplasm. The basal portion of their cytoplasm is often slightly rodged and the cells are so closely pressed together that it is frequently impossible to distinguish their outlines. The secreting cells are disposed in a single layer and, except after active secretion, are so tall as to leave only a very narrow, central, glandular lumen. During secretory activity the cells become shrunken and their cytoplasm more granular. After a period of rest the cytoplasm again becomes clear and vesicular in appearance and the cells are much distended.

The ducts are lined by a double, occasionally triple, layer of somewhat flattened epithelial cells, which rest upon a delicate membrana propria continuous with that of the secreting portion. The gross diameter of the duct is much less than that of the secreting portion of the gland, yet the lumen of the duct is usually the larger. That portion of the duct which is lined by the thin stratified epithelial layer pursues a spiral course through the subcuta-

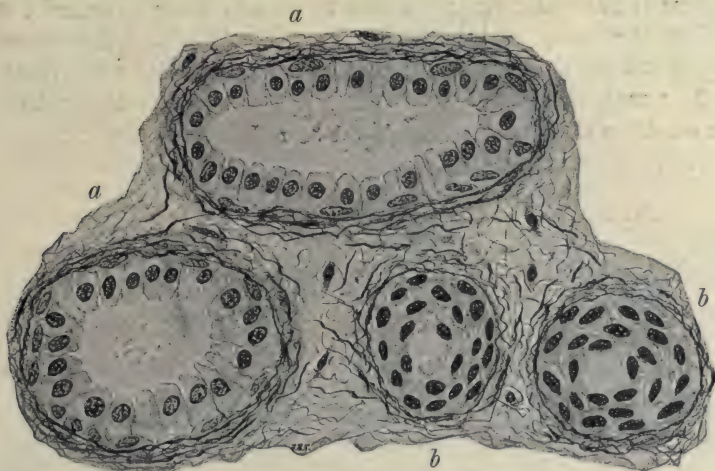


FIG. 182.—SEVERAL COILS OF A SUDORIPAROUS GLAND OF THE HUMAN FINGER. *a*, secreting portions, their lumen containing traces of secretion; *b*, ducts. Hematein and picro-fuchsin. $\times 550$.

neous tissue and the derma. It finally reaches the epidermis, which it enters in the interval between the dermal papillæ (interpapillary portion of the epidermis). Its lining epithelium is continuous with that of the stratum germinativum, and in its course through the epidermis the wall of the duct consists solely of the surrounding epidermal cells. The stratum granulosum and adja-

cent portion of the horny layer in the immediate neighborhood of the duct is invaginated into the stratum mucosum, which is thus considerably thinned by the passage of the duct.

The sweat glands are abundantly supplied with capillary blood vessels and small nerves, which form plexuses about the walls of the coiled portion of the gland, and from which terminal fibrils penetrate the basement membrane and end in contact with the secreting cells.

Development.—The sudoriparous glands first appear in the embryo during the fifth month as solid columnar ingrowths from the stratum germinativum of the epidermis. These processes grow inward through the primitive corium to its junction with the looser subcutaneous tissue. Here the cell columns become thickened and convoluted, and at about the same period their lumen appears. The glandular lumen is not at first connected with the free surface, but as the cells of the germinal layers of the epidermis gradually replace those which are more superficial the epidermal portion of the duct is formed. At about the seventh month the lumen of the duct opens upon the epidermal surface.

The membrana propria of the fundus and dermal portion of the duct are derived from the surrounding connective tissue elements of the mesenchyma.

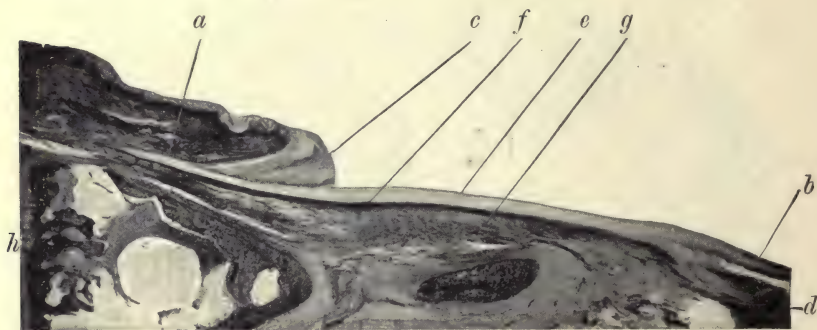


FIG. 183.—THE DORSAL HALF OF THE TIP OF AN INFANT'S FINGER, SHOWING THE NAIL IN SECTION.

a, nail root; *b*, free extremity; *c*, eponychium; *d*, hyponychium; *e*, nail; *f*, stratum mucosum of the nail; *g*, nail bed; *h*, bone. Hematein and eosin. Photo. $\times 23$.

THE NAILS.—The nails are produced by a peculiar modification of the epidermis by which the stratum lucidum becomes greatly thickened while the horny layer is at the same time wanting. The nail is divisible into the *nail body* and *nail root*; the

former comprising the exposed, the latter the hidden portion of the organ. The root of the nail is overhung by a fold of the skin, the thickened horny layer at the margin of which forms an adherent border, the *eponychium*.

The **nail groove** or *sulcus* is included between the overhanging skin and the root of the nail. It is deep at its proximal end but is shallow at the lateral margins of the nail. The distal or free border of the nail projects over the skin at the tip of the finger and the thickening of the horny layer of the subjacent epidermis forms the so-called *hyponychium*.

Finer Structure.—The nail consists of two layers, the superficial stratum lucidum and the deeper Malpighian layer. These are continuous at the border of the nail with the corresponding layers of the epidermis which lines the nail groove. At the distal border, however, the nail proper or thickened stratum lucidum ends in a free margin. The finer structure of these two layers does not essentially differ from that of the corresponding layers of the epidermis.

The *stratum lucidum* in the body of the nail is very thick and its cells are so completely blended with each other through the excessive eleidin production that it is impossible to distinguish their outlines. By maceration in alkaline solutions, however, the outlines of both cells and nuclei may be caused to reappear.

In the nail root the stratum lucidum increases rapidly in thickness as it grows distalward; in the body of the nail this layer is not very materially thickened as it approaches the distal or free margin.

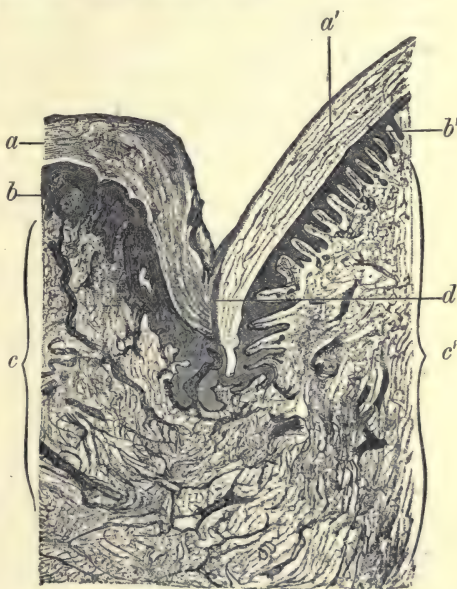


FIG. 184.—TRANSECTION THROUGH THE MARGIN OF A FINGER NAIL.

On the left is the skin, on the right the nail. *a, a'*, horny layer; *b, b'*, germinal layer; *c, c'*, corium; *d*, margin of the nail. Moderately magnified. (After von Brunn.)

The stratum mucosum is of nearly equal thickness in all portions of the nail body. In the nail root it is somewhat thicker and forms the *nail matrix* of Ranvier. In this portion also is a distinct stratum granulosum, a layer which is absent or rudimentary beneath the body of the nail. It is the presence within this layer of numerous keratohyalin granules which renders the root of the nail opaque and thus forms the dull white *lunula* which contrasts with the transparent, eleidin containing, stratum lucidum, which latter layer alone, covers the Malpighian layer of the nail body (Unna).

The Nail Bed.—The nail rests upon a very vascular corium or nail bed (*matrix* of authors) which is continuous with the corium or derma of the skin. The nail bed at the margins of the nail is provided with papillæ as in other portions of the skin, but beneath the body of the nail its surface is raised into longitudinal ridges which possess only very minute secondary papillæ.

Nail Growth.—The growth of the nail occurs almost entirely in the matrix of the nail root. The cells of the stratum germinativum of this portion, having been once formed by active mitosis push obliquely forward and outward toward the nail body. It is thus that the more advanced are constantly carried onward toward the free border. The growth of the nail occurs at the rate of about one thirty-second of an inch per week (Schäfer).

Development.—In the fetus the nail appears as a direct formation of the epidermis, which is very early evidenced by a thickening of the stratum lucidum in the nail area. The nail is therefore at first covered by the superficial epitrichial cells of the cuticle. The nail groove is rapidly formed by an invasion of the mesoblast by the epidermal cells which become piled up at the margin of the groove to form an excessive horny layer or eponychium. At the distal extremity of the nail the superficial cells are also accumulated into a considerable mass which forms a prominent hyponychium. Further growth of the nail pushes its distal margin forward over the eponychium so that the border becomes free shortly prior to birth. The epitrichial cells are then shed and the nail body finally presents, at about the time of birth, its naked stratum lucidum.

THE HAIR.—The structure of the hair will be most readily appreciated if preceded by a brief introductory sketch of its development.

The Hair Germ.—The hairs arise at any time after the third month of fetal life, their earliest anlage appearing as a slightly increased proliferation of the cells of the germinal layer of the epidermis. The further multiplication of the cylindrical cells produces a solid columnar ingrowth of the epidermis which penetrates into, and sometimes through, the primitive derma. The spheroidal cells of the intermediate layer of the epidermis increase in size, assume a vesicular character, and finally by fatty degeneration form the epidermal *hair canal* through which the future hair reaches the surface.

The Hair Column.—The columnar epidermal ingrowths, hair columns or hair pegs, come into early relation with the anlage of the *hair papilla* which is formed by a proliferation of the mesenchymal cells at the tip of the hair column. Further development of the papilla produces an indentation of the advancing hair column and gives rise to a true dermal papilla of considerable size.

The Hair Bulb.—Coincident with the formation of the papilla there is an increased proliferation of the cells of the hair column by which it is surrounded, and which therefore represents the future hair bulb. Two other swellings appear in the hair column; one, the more superficial, forming the anlage of the sebaceous gland, and the other, the deeper, forming the so-called *matrix* of the hair which stands in close relation with the future regeneration of the hair.

The development of the hair papilla produces a slight evagination of the epithelium of the hair bulb, which is just sufficient to redirect the growth of central cells of the hair column toward the cutaneous surface. It is thus that the younger cells which arise by mitosis in the germinal layers of the hair bulb are pushed outward along the axis of the hair column where they form the shaft of the future hair. The growth of the hair from the germinal cells of the hair bulb is accompanied by beginning cornification of the newly formed cells of the primitive hair shaft and of the intermediate cells of the hair column. The growth of the shaft is, however, preceded by enlargement, vesiculation, and fatty degeneration of the central cells of the hair column, thus producing a central canal through which the hair may grow, and which later becomes continuous with the hair canal of the epidermis.

The Hair Follicle.—At this stage the hair column has been differentiated into a peripheral follicle, the primitive *root sheath*,

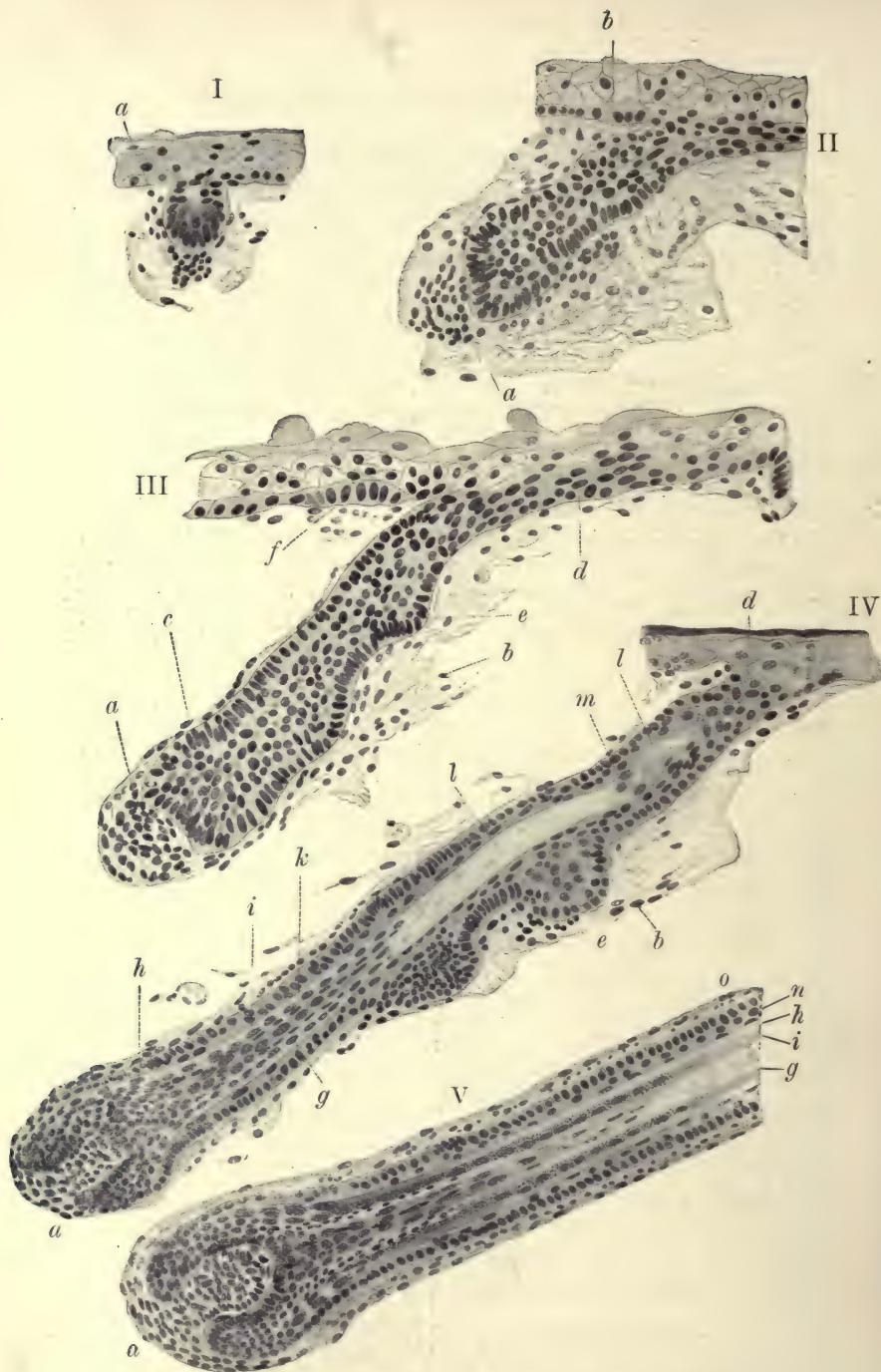


FIG. 185.—FIVE STAGES IN THE DEVELOPMENT OF A HUMAN HAIR.

a, papilla; *b*, arrector pili; *c*, the line is directed toward the primordial shaft; *d*, cells which form the hair canal; *e*, sebaceous gland; *f*, hair germ; *g*, hair shaft; *h*, Henle's layer; *i*, Huxley's layer; *k*, cuticle of the root sheath; *l*, inner root sheath; *m*, outer root sheath in tangential section; *n*, outer root sheath in longitudinal section; *o*, dermal root sheath. $\times 460$. (After Stöhr.)

and a central *hair*. Continued multiplication of the cells in the germinal layer of the bulb pushes the advancing tip of the hair nearer and nearer the surface until it forces its way into the

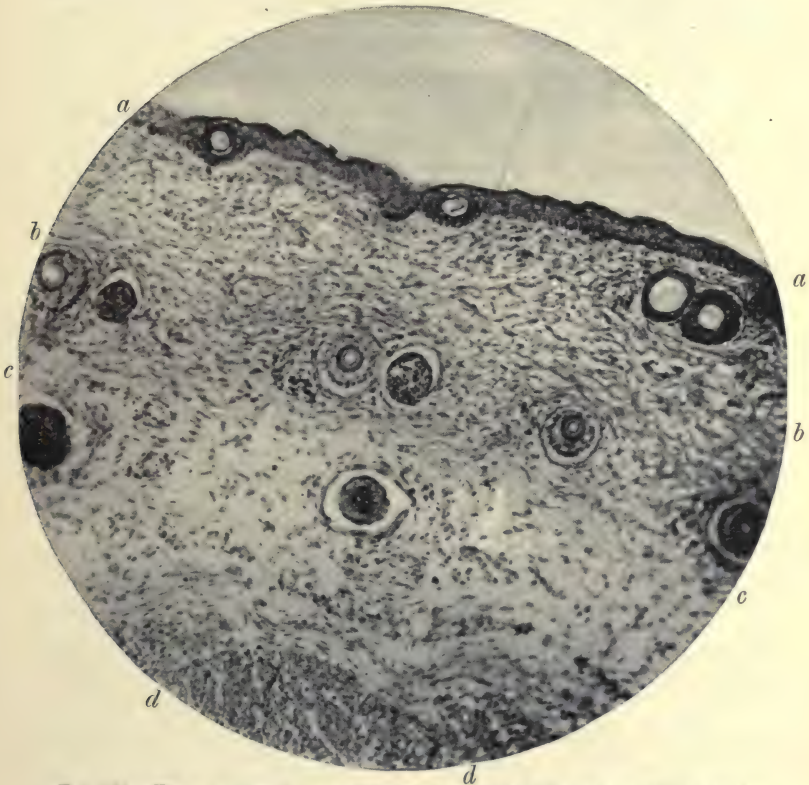


FIG. 186.—FROM A SECTION OF THE SKIN OF AN INFANT'S ARM, SHOWING SMALL IMMATURE HAIR FOLLICLES IN TRANSECTION.

a-a, epidermis; *b-b*, derma; *c-c*, subcutaneous connective tissue; *d-d*, muscle. Hematein and eosin. Photo. $\times 95$.

epidermal hair canal. Finally the thin cuticular covering is ruptured and the eruption of the *hair shaft* occurs.

Further differentiation of the cells of the epidermal root sheath and the formation of a mesenchymal or dermal sheath of connective tissue completes the development of the hair follicle. This process is frequently repeated and results in the formation of new hairs not only during fetal life, but also, in constantly decreasing numbers, throughout childhood and adult life.

THE MATURE HAIR.—Its development teaches that the hair follicle, being formed as it were by an invagination of the epidermis, contains a dermal and an epidermal sheath and that the outer* portion of the latter, being identical with the deeper portion of the epidermis, must possess a close structural resemblance to the rete mucosum, while its inner portion, like the horny layer of the skin, is more or less cornified. There is thus an outer and an inner epidermal root sheath corresponding respectively to the mucous and horny layers of the epidermis; the cornified portion, inner root sheath, becomes progressively thinner toward the hair bulb. The hair, on the other hand, represents an excessively developed horny layer whose rete mucosum is found in the germinal layer of the hair bulb.

The mature hair is divisible into a *hair shaft* or free portion, and a *hair root* or concealed portion. The latter is inclosed within an epidermal and a dermal root sheath which together form the hair follicle.

The Hair Shaft.—Sections of the hair shaft present a thin *cuticle* which consists of delicate horny scales whose free edges are imbricated upward, viz., toward the tip of the hair. Within the cuticle the hair may consist solely of a hair *cortex* formed by flattened and very much elongated horny epithelial cells, which frequently retain the remnant of a nucleus, and whose keratized cytoplasm is often much pigmented; or the axis of the hair may contain enlarged angular cells in which eleidin granules and much pigment are found. In the latter case the hair is said to possess a *medulla*. The medulla is seldom if ever present throughout the entire length of the hair. When present it sometimes contains numerous air bubbles which, together with the absence of pigment, produce the lighter shades of hair peculiar to certain individuals.

In the light of its development it is obvious that the several layers of the hair shaft are comparable to the homologous layers of the horny epidermis, the cuticle, cortex, and medulla of the hair being respectively homologous with the scaly layer, the flattened cell layer, and the eleidin containing layer or stratum lucidum of the epidermis.

The Hair Root.—The root of the hair, except for the fact that it is immediately invested with a hair follicle, does not in any way

* The terms *inner* and *outer* as applied to the hair follicle refer respectively to points nearer or farther from the axis of the hair root.

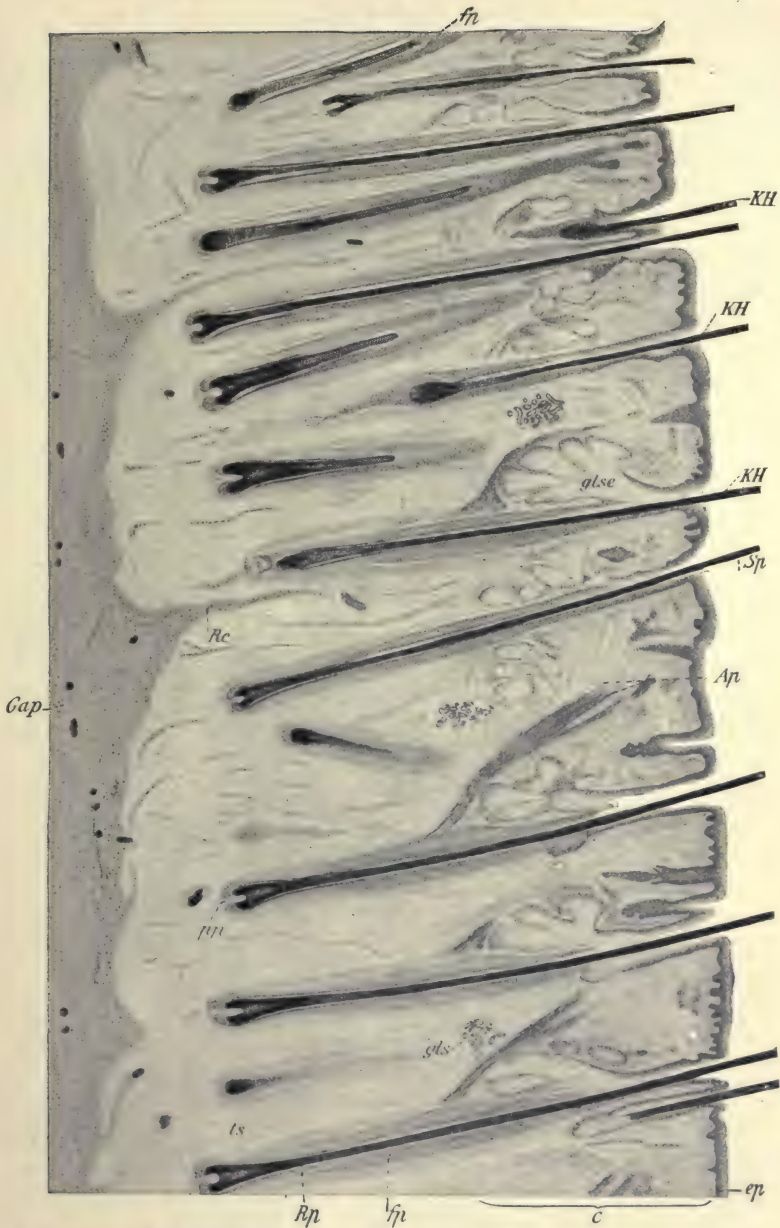


FIG. 187.—FROM A SECTION OF THE HUMAN SCALP.

Ap, arrector pili muscle; *c*, corium; *ep*, epidermis; *fp*, epidermal root sheath; *Gap*, muscular aponeurosis; *gls*, sudoriparous gland; *glse*, sebaceous gland; *KH*, so-called "club-hairs" in various stages of molting and regeneration; *pp*, papilla of the hair; *Rc*, fibrous band in the subcutaneous tissue; *Rp*, hair root; *Sp*, hair shaft; *ts*, subcutaneous adipose tissue. Hematoxylin and eosin. $\times 15$. (After Sobotta.)

differ in structure from the hair shaft. It possesses the same three layers, the medulla, however, being very irregularly developed.

The imbricated cells of its cuticle interdigitate with the similar cells of the cuticle of the root sheath in the deeper half of the follicle; in its superficial half, viz., above the opening of the sebaceous gland, a narrow space intervenes between the cuticle of the hair and that of the root sheath.

The axis of the hair root is always inclined at an angle to the epidermis; it therefore makes with the epidermis an obtuse angle on one side and an acute angle on the other. The arrector pili muscle is always found on the side of the obtuse angle; it therefore, by drawing the hair follicle and its inclosed hair root nearer the perpendicular, causes the erection of the hair. The sebaceous gland is included in the angle between the arrector muscle and the hair follicle.

The Epidermal Root Sheath.—The epidermal root sheath consists of an inner and an outer portion, each of which is here and there divisible into three layers corresponding to the three similar layers of the horny and the mucous portions of the epidermis. In those portions of the follicle and in those individual hairs in which the process of cornification is less advanced these subdivisions can not all be demonstrated, and it is only in the most highly developed hairs that they are typically found. This is in accordance with the structure of the epidermis, in which the subdivisions of its horny and mucous portions are typically found only in the more highly developed portions, e. g., the palms and soles.

Inner Root Sheath.—The *cuticle* of the inner root sheath consists of thin horny epithelial scales which are imbricated downward, viz., toward the hair bulb, and which interdigitate, in the deeper portion of the follicle, with the similar scales of the hair cuticle. The direction of the imbrication explains the removal of the epidermal root sheath when the hair is artificially extracted.

The mid-layer of the inner root sheath, *layer of Huxley*, one or two cells thick, consists of horny cells which are somewhat flattened, and in which the semblance of a nucleus is sometimes present. It corresponds to the flattened cell layer of the epidermis.

The outer layer of the inner root sheath, *layer of Henle*, is frequently wanting or imperceptibly blended with the preceding layer. Its cells are clear and highly refractive and their nuclei can but rarely be demonstrated in the usual microscopical prepa-

rations. The layer is seldom more than one cell deep. It is homologous with the stratum lucidum of the epidermis.

Outer Root Sheath.—The outer root sheath is continuous with the stratum mucosum of the epidermis and therefore contains

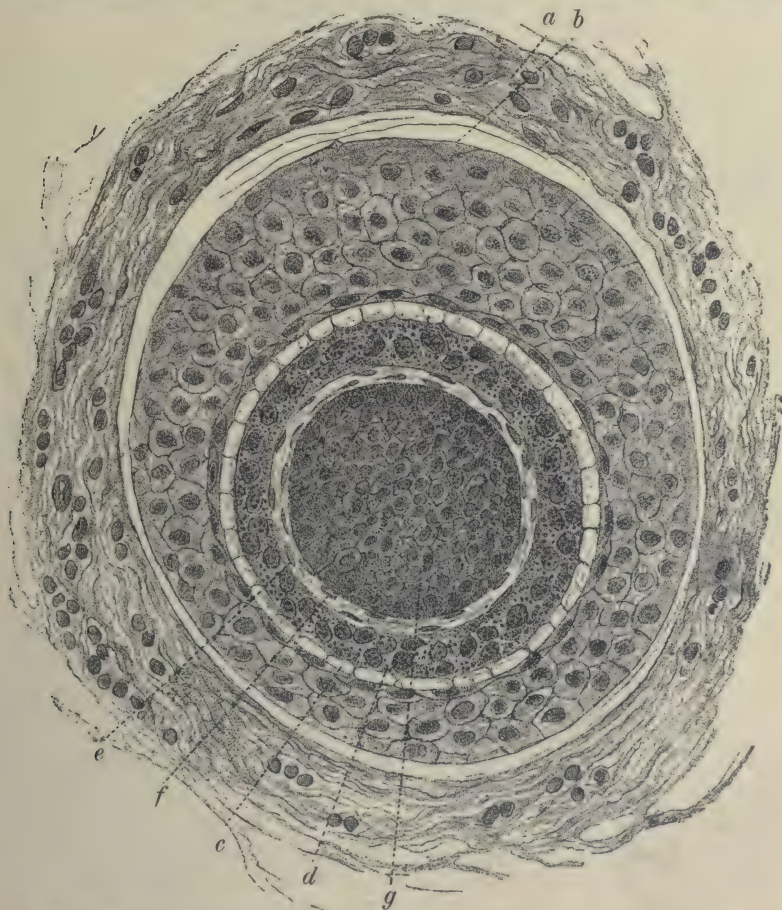


FIG. 188.—TRANSECTION OF A HAIR NEAR THE MIDDLE OF THE ROOT SHEATH.

a, dermal root sheath; *b*, outer margin of the epidermal root sheath—the light space is the glassy membrane, the polyhedral cells form the outer root sheath; *c*, Henle's layer of the inner root sheath; *d*, Huxley's layer; *e*, cuticle of the root sheath; *f*, cuticle of the hair; *g*, cortex of the hair shaft. Highly magnified. (After Kölliker.)

similar cell types. The granular layer, as in the epidermis, is frequently absent or rudimentary, but can be readily demonstrated in hematein-stained sections of the more highly developed hair

follicles. It rests upon a layer, several cells deep, of spheroidal prickly cells. The outermost layer of the outer root sheath is formed by a basal layer of cylindrical cells.

Dermal Root Sheath.—The dermal root sheath presents three layers, an innermost basement membrane or glassy layer, a layer



FIG. 189.—FROM A SECTION OF THE HUMAN SCALP, SHOWING HAIRS IN LONGITUDINAL AND OBLIQUE SECTION.

a, epidermis; *b*, derma; *c*, subcutaneous adipose tissue; *e*, sebaceous gland. A large sweat gland is seen in the deeper edge of the derma near the middle of the figure. Hematein and eosin. Photo. $\times 48$.

of circular connective tissue fibres and a similar layer of longitudinal fibres. These layers are obviously homologous with the basement membrane, the papillary layer, and the reticular layer

of the derma, respectively. The dermal root sheath is, however, devoid of papillæ.

The glassy membrane is a peculiarly thick homogeneous membrane which is chiefly mesoblastic in origin, but whose innermost portion (Köl liker,* Stöhr †) is formed as an exoplasmic product of the adjacent epithelium. This membrane is highly refractive and contains very few connective tissue cells or fibres.

The circular fibres of the dermal root sheath contain interlacing bundles of connective tissue fibres, which are mostly disposed in a ring-like manner. Elastic fibres are absent. Within this layer is a dense anastomosing plexus of capillary blood vessels, together with a rich subepithelial plexus of non-medullated nerve fibres.

The longitudinal fibres of the connective tissue root sheath also form interlacing fibre bundles, most of which are somewhat obliquely disposed. The bundles are coarser than those of the preceding layer and contain a few elastic fibres. This portion of the root sheath contains many small blood vessels and nerves which supply the plexuses of the circular layer.

Atypical Portions of the Hair Follicle.—As already indicated, the hair follicle presents some structural differences at various levels. The typical arrangement is found only in the mid-portion of the follicle.

In its superficial portion the hair lies free in the follicular lumen, the interval between it and the inner root sheath being only partially occupied by the fatty secretion of the sebaceous gland which enters the lumen of the follicle at the deeper portion of its middle portion. At this level also, the root sheaths of the hair offer a gradual transition from their typical structure to that of the dermal and epidermal layers with which they are continuous.

The hair bulb likewise differs prominently from the typical structure of the hair root. In this portion the Malpighian layers are very highly developed at the expense of the horny layers. It is, therefore, in this portion that growth is most active. The cells of this region are often deeply pigmented. The increased size of the Malpighian layer, moreover, produces a distinct bulging of the follicle, which incloses the hair papilla and results in the peculiar bulbous shape of the extremity of the hair follicle.

* Handbuch.

† Anat. Hefte, 1903.

The Hair Papilla.—The structure of the hair papilla is identical with that of the vascular papillæ of the derma except that it is constructed upon a much larger scale. It consists of a conical or club-shaped elevation of connective tissue which indents the extremity of the hair bulb. It contains an abundant plexus of capillary blood vessels and a rich supply of non-medullated nerves. It also contains an undue proportion of connective tissue cells.

Regeneration of the Hair.—Hairs are being continuously shed and regenerated, the average life of a hair of the scalp being stated as sixteen hundred days (Stöhr *). The shedding of a hair is first heralded by an atrophy of its papilla and a cornification of its bulb. Growth ceases, and the hair, firmly adherent to its root sheath, is gradually carried, by the continued growth of the latter, nearer and nearer the surface of the skin. Its excursion leaves behind a narrowed cell column which still unites the hair with its former papilla.

From this rudiment a new hair germ may form (Unna †), a new papilla develop, and the resulting hair grows toward the surface in the path of the molting hair, its eruption being preceded by the falling of its predecessor. The formation of the new hair germ very probably occurs at a point nearly corresponding with the insertion of the arrector pili muscle, where there is a swelling of the root sheath which has been already mentioned as the *matrix* of the hair follicle. This matrix appears very early in the development of the hair, but remains quiescent until regeneration becomes necessary.

Shed hairs are also compensated for by new formation from hair germs appearing at the germinal border of the epidermis, the process proceeding in the manner already described for the development of the hair.

THE SEBACEOUS GLANDS.—These are compound saccular glands which may be subdivided into two classes, (1) those whose ducts open into the hair follicles, and (2) those whose ducts open upon the free surface of the epidermis. The former are by far the more numerous; the latter occur in the skin of the face, red margins of the lips, labia minora, glans penis and prepuce (Tyson's glands), and the Meibomian glands of the eyelids. With the above exceptions the distribution of the sebaceous glands is coextensive with that of the hairs. They are therefore absent from the palms of the hands and soles of the feet.

* Text-Book of Histology.

† Arch. f. mik. Anat., 1876.

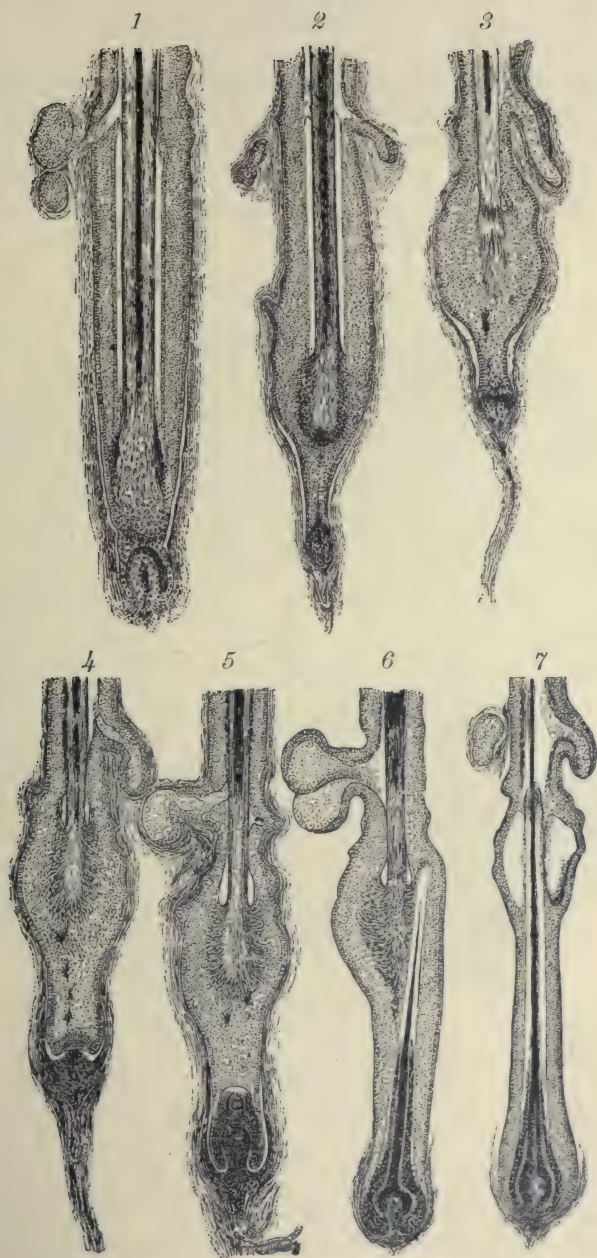


FIG. 190.—REGENERATION OF A HAIR.

Only the follicles and the inclosed portion of the hair shafts are represented. The various stages are numbered in order. (After Unna.)

A sebaceous gland consists of a dilated saccular fundus, a constricted neck, and a short and narrow duct. Occasional glands are formed by a single saccule, but more frequently they are compound, the several saccules opening by a single short duct which is lined by flattened cells. In the Meibomian glands the secreting

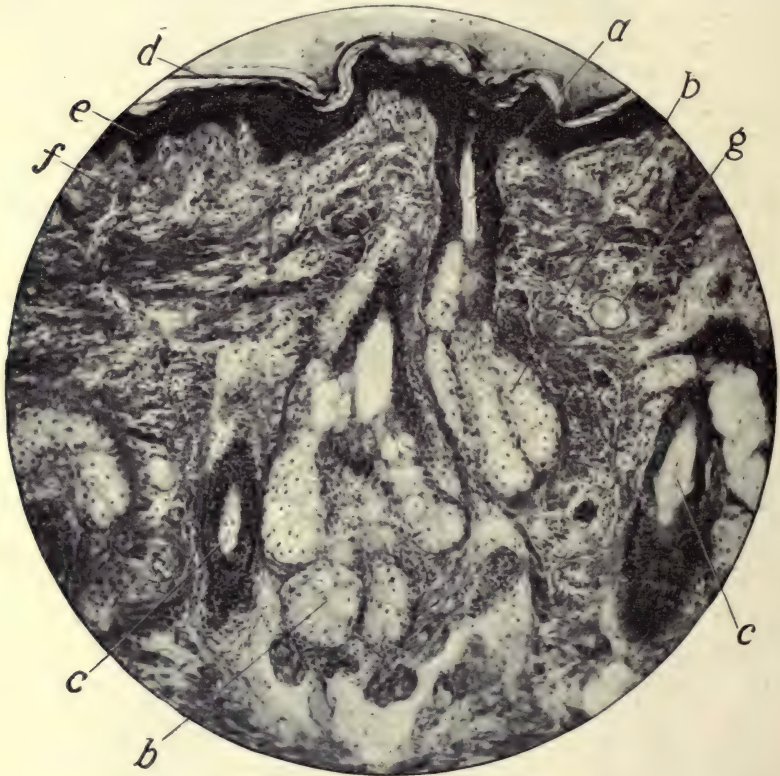


FIG. 191.—SEBACEOUS GLANDS IN THE SCALP OF A CHILD.

a, hair follicle; *b*, sebaceous gland; *c*, hair follicles in oblique section; *d*, horny layer of the epidermis; *e*, Malpighian layer; *f*, derma; *g*, blood vessel. Hematein and eosin. Photo. $\times 83$.

saccules are connected with the long excretory duct by means of a short intercalary duct. The fatty secretion of the sebaceous glands, sebum, is formed by the direct disintegration of the protoplasm of the glandular epithelium.

The saccules of the sebaceous glands are invested by a thin connective tissue tunic and a delicate basement membrane. They

are embedded in the subcutaneous fat or in the deeper part of the corium near the hair follicle. The glands are so disposed as to be included within a triangular space beneath the corium, which is bounded by the arrector pili muscle and the hair follicle. The saccules are lined by several layers of polygonal epithelial cells the outermost of which are cylindrical and rest upon the basement membrane.

In the peripheral layers the lining epithelial cells multiply so actively that the daughter cells are pushed inward until they fill the entire saccule. During this excursion they are progressively farther and farther removed from their source of nutrition, and as they approach the outlet or duct of the saccule a process of fatty degeneration appears within the cell, by which its protoplasm becomes changed into a granulo-fatty mass. The accumulated product of this degeneration and final disintegration of the epithelial cells forms the secretion of the gland. Continued cell multiplication at the periphery maintains the integrity of the organ.

Development.—The sebaceous glands are developed as minute epithelial buds from the sides of the hair columns or from the deeper surface of the epidermis. These buds soon assume the characteristic flask-like shape and later become hollowed out by fatty degeneration of their central cells. By this process also their lumen is eventually made continuous with that of the follicle. Secondary saccules of the sebaceous glands are developed in a similar manner by outgrowing germs which appear near the constricted neck portion of the primary saccule.

BLOOD SUPPLY OF THE SKIN

The larger arteries supplying the skin lie in the subcutaneous tissue. From these vessels branches pass toward the surface, giving off lateral twigs to the rich capillary plexuses in the subcutaneous connective and adipose tissues and about the sweat glands, hair follicles, and sebaceous glands. These arteries continue their course to the deeper part of the corium, where they form an anastomosing plexus of small vessels. Branches from this plexus pass to the papillary layer, where they form a second plexus from which terminal arteries are distributed to the capillaries of the papillæ.

The distribution of the veins is similar to that of the arteries. The primary plexus is found in the papillary layer; occasionally

a second plexus immediately underlies the first, and from these, venules pass to the deeper part of the corium, whence after free anastomosis they proceed to the subcutaneous tissue, collecting on the way the venules returning from the hair follicles and

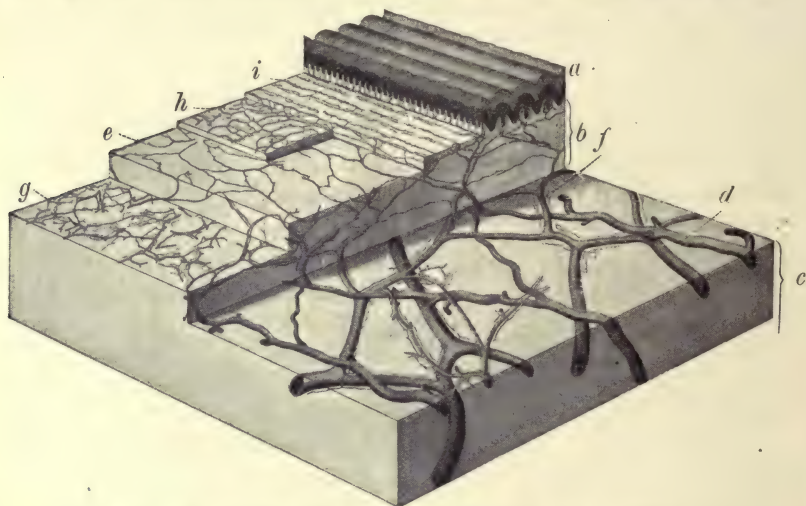


FIG. 192.—RECONSTRUCTION OF THE CUTANEOUS BLOOD VESSELS.

a, epidermis; *b*, derma; *c*, subcutaneous tissue; *d*, deep, and *e*, superficial arterial plexus; *f-i*, successive venous plexuses. $\times 9\frac{1}{2}$. (After Spalteholz.)

secreting glands, and from the subcutaneous connective tissue. The very rich capillary network in the papilla of the hair bulb is worthy of special mention.

The lymphatic vessels of the skin begin as a terminal lymphatic plexus in the corium, which collects the lymph from the tissue spaces of both derma and epidermis. The vessels of this plexus communicate with a subcutaneous lymphatic plexus of larger vessels which follow the course of the blood vessels on their way to reach the neighboring groups of superficial lymphatic glands.

NERVE SUPPLY.—The skin is abundantly supplied with large nerve trunks which find their way along the subcutaneous fat and send branches directly to the larger blood vessels, the hair follicles, the sebaceous and sudoriparous glands, to the corpuscles Pacini, Ruffini, and Golgi-Mazzoni, and to the end bulbs of Krause, which lie in the connective tissue.

In the cutis vera the nerve trunks form a plexus of delicate fibre bundles in the reticular layer, with a secondary, more closely

meshed plexus of finer nerve bundles in the papillary layer. From these plexuses fibrils are distributed to the smaller blood vessels and to the papillæ, where many of them end in tactile corpuscles. Still other fibrils penetrate the epidermis, and, becoming more or less varicose, terminate as naked fibrils between the cells of the stratum germinativum, many of them being distributed to the tactile cells of Meissner.

In the region of the hair follicle small branches form a network of fibrils in the dermal root sheath, which surrounds the follicle as far outward as the opening of the sebaceous glands. Branches (pilomotor nerves) are also distributed to the arrector pili muscles.

In the sudoriparous glands the nerves form a fine plexus about the membrana propria (epilamellar plexus), from which naked axis cylinders penetrate the basement membrane and terminate between the secreting cells.

CHAPTER XIV

THE RESPIRATORY SYSTEM

THE respiratory system may be said to comprise a true respiratory organ, the pulmonary alveoli, in which the interchange of gases between the air and the blood occurs, and a system of duct-like passages leading thereto, which, beginning with the nasal cavity, successively includes the naso-pharynx, larynx, trachea, and bronchi of gradually diminishing caliber, and which finally ends in the terminal bronchioles leading to the pulmonary alveoli or air saccules.

The arrangement of these several portions of the respiratory system has been frequently compared to the structure of the tubulo-acinar secreting glands. From this point of view the larynx and trachea form the duct stem of the gland, the bronchi form the branching interlobular ducts, and the terminal bronchioles end in the numerous acinar air saccules of the lung.

THE NASAL CAVITY.—This cavity is bounded by a cartilaginous and bony wall and is lined by a mucous membrane which, according to the nature of its epithelium, may be divided into three portions: (1) the vestibule, (2) the respiratory portion, and (3) the olfactory portion.

The **VESTIBULE** of the nose corresponds very closely to the cartilaginous portion of the nasal wall. Its mucous membrane is continuous anteriorly with the skin and posteriorly with the mucous membrane of the respiratory portion. The vestibule is lined by stratified squamous epithelium, which offers a gradual transition from the moist respiratory epithelium to the dense horny epidermis of the skin. Near its external orifice are numerous coarse stiff hairs, vibrissæ, connected with which are many sebaceous glands. Some of these glands also open directly upon the surface of the mucous membrane.

The fibrous tunica propria of the vestibule is continuous with the corium of the skin, and in it are embedded the deeper portions

of the vibrissæ and the secreting portions of the sebaceous glands. By its deeper surface the tunica propria is closely attached to the perichondrium of those plates of hyaline cartilage which form the septum and alæ of the nose.

The **RESPIRATORY PORTION** of the nasal mucous membrane (Schneiderian membrane) clothes the middle and inferior meatus of the nose. It is continuous anteriorly with the mucous membrane of the vestibule, above with the olfactory mucous membrane, and posteriorly with that of the naso-pharynx. The respiratory region is lined by columnar ciliated epithelium of the pseudo-stratified type, which also contains many mucus secreting, goblet cells.

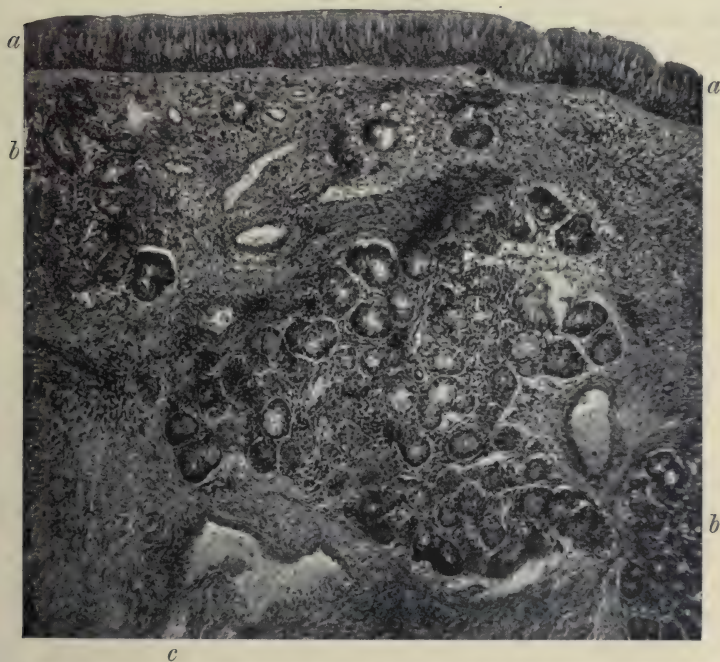


FIG. 193.—FROM A SECTION OF THE MUCOUS MEMBRANE OF THE RESPIRATORY REGION OF THE HUMAN NOSE.

a-a, ciliated epithelium; *b, b*, secreting glands; *c*, blood vessel. Hematein and Congo red. Photo. $\times 185$.

The epithelium rests upon a distinct basement membrane which reacts to the specific stains for elastic tissue. The tunica propria consists of a very vascular connective tissue; it varies much in thickness in different portions. It is thinnest in the

accessory sinuses and is thickest where it covers the turbinal bones and the adjacent portions of the nasal septum. The tunica propria is richly supplied with both mucous and serous glands. The smaller ones, in the thinner portions of the mucous membrane, are somewhat convoluted; the larger and more numerous are tubulo-acinar glands. Many of the latter are mixed glands containing both mucous and serous acini. They produce an abundant secretion.

The Schneiderian membrane is in all portions extremely vascular, many of its vessels having very thin walls. The thicker portions over the turbinals and the septum are typically *erectile*. The dense connective tissue of these portions is permeated with broad venous channels which are surrounded by bands of smooth muscle. Other muscular bundles are longitudinally distributed. The small arteries are contained within the fibro-muscular stroma.

The subepithelial portion of the tunica intima contains fine interlacing bundles of connective tissue and many capillary blood vessels. Here and there it is also infiltrated with leucocytes and occasional very minute lymphoid nodules are found. The lymphatics of the Schneiderian membrane lead posteriorly to the lymphatic nodules of the naso-pharynx.

The **OLFACTORY PORTION** of the nasal mucous membrane, **THE OLFACTORY ORGAN**, lines the superior meatus, and its irregular border here and there invades the upper portion of the middle meatus. It consists of a fibrous tunica propria and a clothing of neuro-epithelium. The tunica propria contains elastic as well as white connective tissue fibres, and many small tubulo-acinar secreting glands, the *olfactory glands* of Bowman. Beneath the epithelium is an indistinct basement membrane.

The neuro-epithelium contains three intermingled cell types, the sustentacular, olfactory, and basal cells.

The **Sustentacular Cells** are columnar ciliated epithelial cells which possess a distinct cuticular margin. Their nuclei are ovoid, and, since they lie at the same level, they form a continuous superficial *zone of oval nuclei*. The deep ends of the cells are often branched; they interlace with one another and with the processes of the olfactory and basal cells. The cytoplasm of the sustentacular cells is finely granular and contains a yellow pigment.

The **Olfactory Cells** occupy a unique position among neuro-epithelial cells in that they are true nerve or ganglion cells. They

possess a small cytoplasmic body and two processes, a distal and a central. Their nuclei are spherical and are disposed in several rows beneath the nuclear zone of the sustentacular cells; thus they form a broad *zone of spherical nuclei*. The distal process of

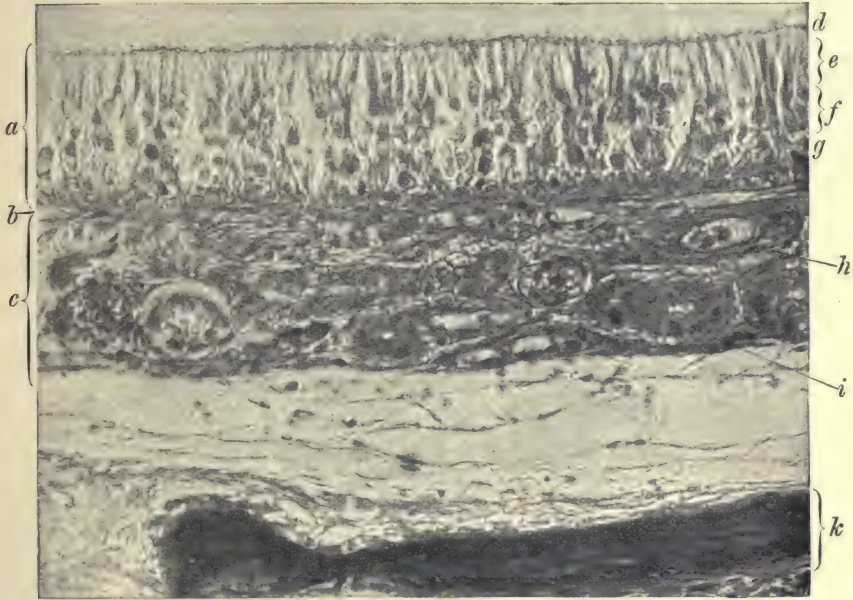


FIG. 194.—THE OLFATORY MUCOSA OF A CAT.

a, epithelium; *b*, basement membrane; *c*, corium; *d*, cuticle; *e*, sustentacular cell layer; *f*, olfactory cell layer; *g*, basal cells; *h*, blood vessel; *i*, a tubule of Bowman's glands; *k*, bone. Hematein and picro-fuchsin. Photo. $\times 270$.

the olfactory cell projects as a slender filament whose free end, carrying several fine cilia, reaches the surface of the membrane through a pore-like opening in the cuticular membrane which is formed by the cuticle of adjacent sustentacular cells. The central process of the olfactory cell penetrates to the tunica propria and becomes a non-medullated nerve fibre of one of the many rami of the olfactory nerve; it passes to the olfactory bulb, where its terminal arborization with the dendrites of the mitral cells forms the olfactory glomeruli.

The **Basal Cells** are flattened cells which form the deepest nuclear zone of the olfactory neuro-epithelial layers. Their cytoplasm is finely granular and their nuclei are ovoid or flattened.

Frequently they send a short process between the branched ends of the sustentacular cells.

Many small **nerve trunks** occur in the tunica propria. The great majority of these are non-medullated and are formed by the central processes of the olfactory cells. Several of the smaller superficial fibre bundles unite in the deeper part of the tunica propria to form one of the small olfactory nerves. A few medullated fibres, derived from the trigeminus, are also found in the tunica propria; they distribute their terminal branches to the

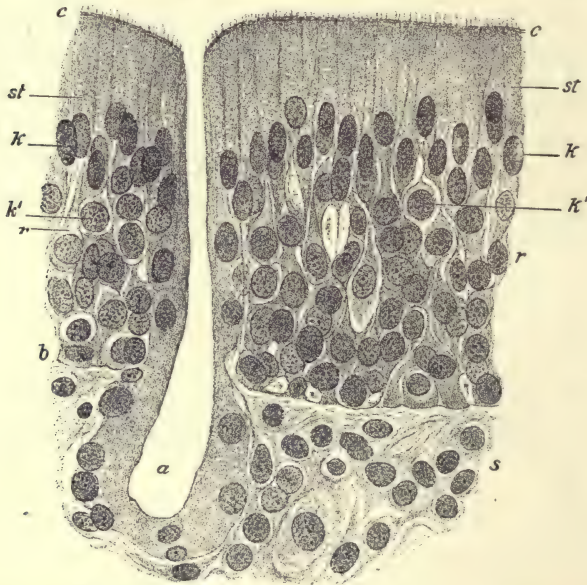


FIG. 195.—THE OLFACTORY MUCOUS MEMBRANE.

a, duct; *b*, basal cells; *c*, cuticular border with olfactory cilia; *k*, nuclei of the sustentacular cells; *k'*, nuclei of the olfactory cells; *r*, layer of olfactory cells; *s*, corium, containing connective tissue cells and nerve fibres; *st*, sustentacular cells. $\times 465$. (After Kölliker.)

blood vessels, and, by fine sensory filaments which end between the epithelial cells, to the neuro-epithelial layer.

The **blood vessels** of the olfactory mucous membrane are abundant. Their capillary plexuses form several layers in the tunica propria, and their veins mostly empty, through the ethmoidal veins, into the superior longitudinal sinus—a most significant fact. On the other hand the veins of the respiratory region return their blood to the internal maxillary vein, while some of those of the

vestibule anastomose with the radicals of the facial vein which supply the adjacent skin.

The **lymphatics** of the olfactory region can be readily injected from the sub-dural spaces of the meninges. They form a network in the connective tissue of the tunica propria.

THE NASO-PHARYNX.—This cavity, like that of the nose, is limited by a bony wall. Its mucous membrane is continuous anteriorly with that of the respiratory portion of the nose, and posteriorly with that of the oro-pharynx. The structure of its mucous membrane resembles that of the Schneiderian membrane, but its dorsal wall, in addition to the ciliated epithelium, the thin-walled blood vessels, and the numerous

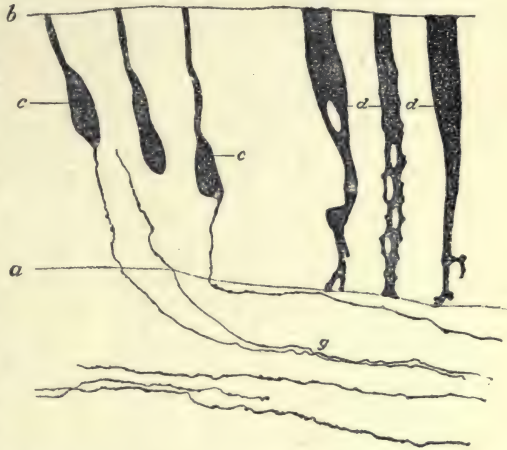


FIG. 196.—VERTICAL SECTION OF THE OLFACTORY MUCOSA OF A KITTEN.

a, deep, and b, superficial border of the epithelium; c, olfactory cells; d, sustentacular cells; g, olfactory nerve fibres in the corium of the mucosa. Golgi stain. $\times 325$. (After Kölliker.)

secreting glands, contains many small nodules of lymphoid tissue. These nodules form a considerable mass, the *pharyngeal tonsil*.

The ciliated epithelium of the naso-pharynx is also continuous with the lining epithelium of the Eustachian tube. The tunica propria is firmly adherent to the bony wall of the dorsal surface, but is more loosely attached laterally and ventrally to the pharyngeal and palatine muscles.

THE LARYNX.—The wall of the larynx is formed by several large plates of hyaline cartilage—thyroid, cricoid, and arytenoid cartilages—which are firmly united by ligamentous bands of fibrous tissue; the cartilaginous wall incloses a mucous membrane of considerable thickness.

The larger **cartilages** are of the hyaline variety and are prone to ossify in adult life. The tips of the arytenoids, the cornicula of Santorini, the cuneiform cartilages of Wrisberg, and the epi-

glottis are of the elastic variety of cartilage, and, though frequently much infiltrated with fat, are not, like the hyaline cartilages, subject to ossification. The intrinsic muscles of the larynx, taking



FIG. 197.—A VERTICAL SECTION THROUGH THE LATERAL WALL OF THE HUMAN LARYNX.

a, cartilage; *b*, laryngeal mucosa, clothed with ciliated epithelium; *c*, transection of the vocal cord, in this region the mucosa is clothed with stratified epithelium; *d*, ducts of mucous glands; *e*, lymphoid nodule; *f*, muscle; *g*, mucous glands; *h*, submucosa; *i*, blood vessel; *V*, ventricle of the larynx. Hematein and eosin. Photo. $\times 8$.

origin from these cartilages, pursue their course beneath the mucous membrane.

The upper portion of the larynx, including the greater part of

the epiglottis, as far as the false vocal cords is lined by stratified epithelium which is continuous with that of the pharynx.

The **epithelium** of the vocal cords and that covering the anterior surface of the arytenoids is also of the stratified squamous variety. The remaining portions of the larynx, including the base of the epiglottis on its laryngeal surface, the ventricle, and the entire portion below the level of the true vocal cords, are lined by columnar ciliated epithelium of the pseudo-stratified type. The ciliary motion is directed toward the pharynx. The epithelium rests upon a basement membrane which is less highly developed than in other portions of the respiratory tract.

The **tunica propria** consists of connective tissue in which are many small tubulo-acinar mucous glands. These are most abundant in the region of the ventricle and the false vocal cords. In this region also there is much diffuse lymphoid tissue, and the lateral and dorsal wall contains several lymphatic nodules which are so constant in their appearance as to have led Fränkel* to describe them as forming a "laryngeal tonsil." Occasionally, however, lymphatic nodules are not present in the mucous membrane of the human larynx. The deeper portion of the tunica propria in certain parts, e. g., in the false vocal cords, contains a few muscle fibres in addition to those of the named muscles of the larynx. The false vocal cords and the aryteno-epiglottic folds contain loose fibrous tissue and frequently much fat.

The true **vocal cords** are formed by dense bands of elastic and a few white fibres which are covered by a mucosa clothed with stratified epithelium. Their free margin is sharply defined; at their attached margin, however, they blend indistinctly with the tunica propria. The free margin of the vocal cords has no connective tissue papillæ on the surface of the tunica propria, but toward the trachea superficial papillæ of connective tissue project into the deeper surface of the stratified epithelium.

The mucous membrane of the larynx is freely supplied with blood vessels and lymphatics. The latter terminate in the deep cervical lymphatic nodes. The nerve fibres form an abundant plexus in the laryngeal mucosa, from which motor fibres are distributed to the muscles and sensory fibres to the epithelium. The latter end in fine fibrils between the cells of the lining epithelium. In the stratified epithelium, especially that of the epiglottis, small taste buds are also found; none, however, occur on the vocal cords.

* Arch. f. Laryngol. u. Rhinol., 1893.

THE TRACHEA.—The wall of the trachea somewhat resembles that of the larynx. It consists of three layers:

1. The mucous membrane.
2. The submucosa.
3. The fibro-cartilaginous coat.

The **mucous membrane** presents slight longitudinal folds, and is lined by columnar ciliated epithelium, like that of the larynx, which rests upon a delicate basement membrane. The **tunica propria** includes a thin inner layer of connective tissue which is richly supplied with small blood vessels and infiltrated by many

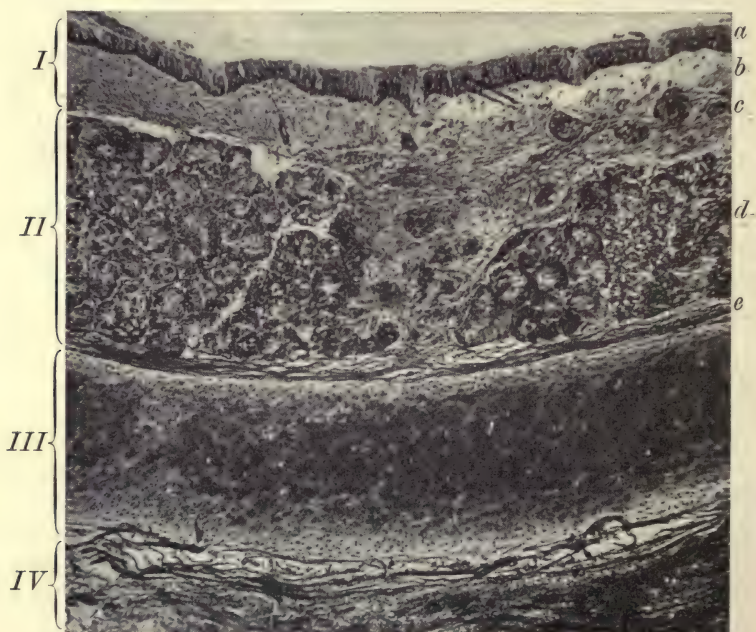


FIG. 198.—TRANSECTION OF THE WALL OF A CHILD'S TRACHEA.

I, mucosa; *II*, submucosa; *III*, cartilage; *IV*, outer fibrous coat; *a*, columnar ciliated epithelium; *b*, tunica propria; *c*, layer of elastic fibres; *d*, mucous glands; *e*, perichondrium. Hematein and eosin. Photo. $\times 90$.

leucocytes, and an outer layer of elastic tissue most of whose fibres are longitudinally disposed. The elastic layer begins in the region of the vocal cords in the larynx and is continuous below with the similar layer of the bronchial mucous membrane. Elastic fibres are more numerous in the trachea of the lower mammals than in that of man.

The **submucosa** consists of loose areolar tissue which contains many small tubulo-acinar mucous glands. The ducts of these glands penetrate the mucosa and open upon the free surface of the trachea. They supply an abundant mucous secretion. This coat also contains the larger blood vessels and nerves which are destined for the supply of the mucosa.

The **fibro-cartilaginous coat** is formed by the C-shaped "ring cartilages" of the trachea which are firmly united to one another by ligamentous membranes of fibrous tissue continuous with the perichondrium of adjacent cartilage plates. The cartilages are of the hyaline variety and are subject to more or less ossification as age advances. They rarely overlap each other, so that but a single plate of cartilage forms the wall at any given point. Their borders are irregular, and horizontal sections near the upper or lower margin of the cartilage, frequently pass through several projections, which, unless properly interpreted, would lead one to infer that the cartilaginous ring was incomplete.

The interval between the ends of the C-shaped cartilage rings is occupied by a membrane of smooth muscle whose transverse fibres unite the adjacent ends of the cartilages. The muscle fibres are inserted into the perichondrium of the cartilages. Many of the fibres are obliquely, and a few of the outermost are longitudinally disposed. This muscular portion of the tracheal wall forms the so-called *trachealis muscle*. The mucous membrane and submucosa of this portion of the trachea are unusually thick and their mucous glands are exceptionally large. The loose fibrous tissue which invests the outer surface of the cartilaginous coat contains many small sympathetic nerve trunks and ganglia.

THE BRONCHIAL TUBES AND PULMONARY ALVEOLI.—

At the root of the lung the trachea divides into a primary bronchus for each lung. By repeated subdivisions—the earliest branches being given off at acute angles, the later ones at more obtuse



FIG. 199.—MUCUS-SECRETING, TUBULO-ALVEOLAR GLAND OF THE HUMAN TRACHEAL MUCOSA.

Reconstruction. $\times 200$.
(After Maziański.)

angles—the smaller and smaller bronchi finally end in minute terminal bronchioles which lead through the alveolar ducts to the pulmonary air sacs or alveoli.

The wall of the largest **BRONCHI** is similar in structure to that of the trachea, but in bronchial tubes which are two or three divi-



FIG. 200.—A LARGE BRONCHUS OF THE PIG'S LUNG.

a, pulmonary artery; *b*, pulmonary vein; *c*, pulmonary alveoli; beneath *d*, a terminal bronchiole with its infundibulum and atrium is seen. Hematein and eosin. Photo. $\times 10$.

sions removed from the primary bronchi the plates of cartilage are no longer C-shaped, and a complete muscularis mucosæ, within the cartilages, forms the outermost boundary of the mucous membrane.

In such tubes—typical bronchi—the wall, as in the trachea, comprises:

1. A mucous membrane.
2. A submucosa.
3. A fibro-cartilaginous coat.

The **mucous membrane**, a continuation of that of the trachea, is lined by tall, columnar, pseudo-stratified, ciliated epithelium which rests upon a distinct elastic basement membrane. The epithelium is thrown into wavy longitudinal folds. The tunica propria is extremely vascular; it possesses an abundant supply of thin-walled veins of small caliber, together with many lymphatic vessels. Its connective tissue forms a delicate fibrous reticulum in the meshes of which are many lymphatic corpuscles. The outer portion of the tunica propria contains bundles of fine longitudinal elastic fibres, which form a complete layer about the tube. This elastic layer is thickest opposite the ridges and thinnest opposite the troughs of the epithelial waves.

The outer boundary of the mucous membrane contains a well-developed *muscularis mucosæ* composed of interlacing bundles of circular smooth muscle fibres. This layer forms a complete muscular coat which is here and there pierced by the ducts of mucous glands whose secreting portions lie in the submucosa.

The **submucosa**, by its broad-meshed areolar tissue, loosely unites the mucous membrane to the cartilage plates. This coat contains the larger blood vessels, nerves, and lymphatics which are distributed to the mucosa. It also contains the secreting portions of many tubulo-acinar mucous glands, which occur in groups that in the larger bronchi almost completely surround the tube. The number and size of these glands is in direct proportion to the size of the bronchus. The efferent ducts of the mucous glands penetrate the muscularis mucosæ and open upon the free surface in the interval between adjacent folds of the epithelial lining. In the tunica propria the ducts possess ampullary dilatations which are lined by ciliated cells and contain portions of the mucous secretion.

The **fibro-cartilaginous coat** is formed by a dense fibrous membrane in which the cartilages are embedded. The plates of hyaline cartilage vary much in number and size, being more or less highly developed in proportion to the size of the bronchial tube. They possess at all times a somewhat crescentic shape. In the larger bronchi three or four cartilage plates with overlapping

edges encircle the entire tube. In the lower mammals, e. g., the pig, these overlapping cartilages are so highly developed that the plates often lie three or four deep; in man they are rarely more



FIG. 201.—A BRONCHUS FROM THE HUMAN LUNG.

a, lining epithelium; *b*, duct of a mucous gland; *c*, muscularis mucosæ; *d*, accumulated mucus, etc., bathing the surface of the epithelium; *e*, mucous glands; *f*, hyaline cartilage; *g*, outer fibrous coat; *h*, pulmonary alveoli. Hematein and eosin. Photo. $\times 34$.

than one or two deep. As the bronchi diminish in size by division, the cartilage plates are no longer of sufficient size to completely encircle the wall but leave broad intervals in which this coat is only represented by fibrous tissue. In tubes of a diameter of 0.85 to 1 mm., *bronchioles*, the cartilages entirely disappear, and in these or somewhat smaller bronchioles the mucous glands are, likewise, no longer found.

The outer surface of the cartilages is invested with a clothing of loose fibrous tissue of varying thickness—sometimes known as the *outer fibrous coat*—in which the branches of the pulmonary artery and veins and also many nerve trunks and ganglia are found. In the larger bronchi the two vessels, pulmonary artery and pulmonary vein, are found on opposite sides of the tube; in the bronchioles only one vessel, the artery, is in relation with the tube, the vein pursuing an independent course within the pulmonary tissue.

Near the root of the lung many small lymphatic glands are found in the outer fibrous coat. In the smaller bronchi these are represented by single lymphatic nodules which, it is important to note, are always found in the fibrous connective tissue which forms the outer portion of the bronchial wall. The bronchial lymphatic glands and nodules are deeply pigmented, the volume of the pigment being dependent upon the age and occupation of the individual. It is apparently derived by absorption from the surface of the bronchi and is therefore absent in infancy, deficient in youth, abundant in adult life, and especially abundant in those individuals whose occupations have necessitated the inhalation of a dusty atmosphere.

The small **BRONCHIOLES** possess neither cartilage, mucous glands, nor lymphatic nodules. Their epithelium, though still ciliated, is low—short columnar, or, in the smaller bronchioles, cuboidal. The tunica propria contains many lymphatic corpuscles and the elastic tissue forms an almost complete layer of longitudinal elastic fibres.

The muscularis mucosæ is relatively more highly developed than in the larger bronchi; it completely encircles the wall and is invested with an adventitious layer of fibrous tissue which contains the small arteries, nerves, lymphatics, a capillary plexus with elongated meshes, and occasional venules.

The fibrous coat of the bronchiole here and there blends with the fibrous bands of interlobular tissue and is in contact with the

adjacent pulmonary alveoli. The terminal portion of each bronchiole enters the apex of a pulmonary lobule and divides into several so-called terminal bronchioles (*"respiratory bronchioles"* of Kölliker).

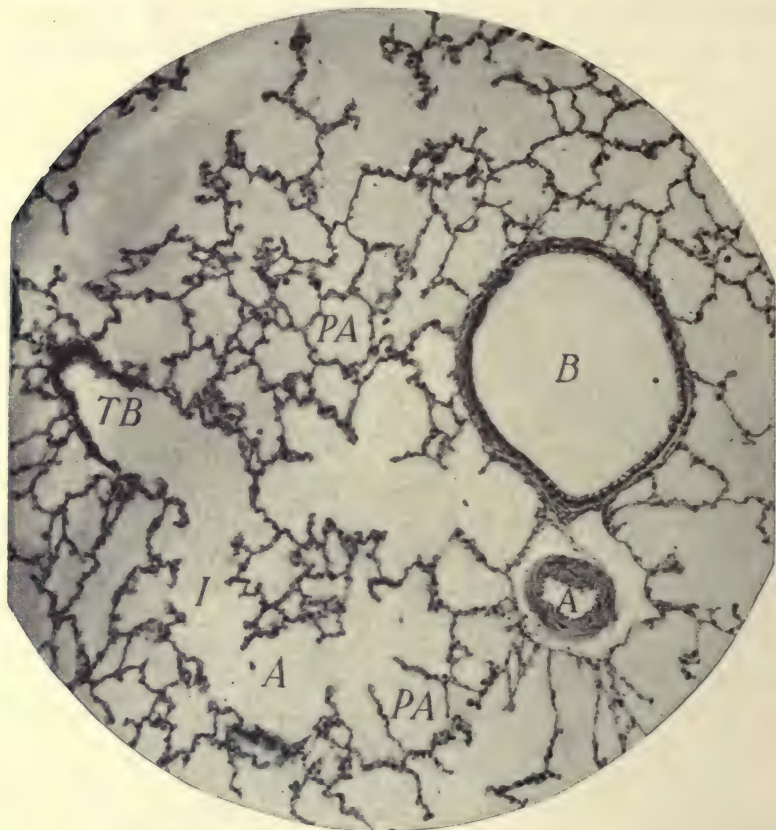


FIG. 202.—FROM A SECTION OF A CHILD'S LUNG.

B, bronchiole in transection, with its adjacent pulmonary artery, *A*; *TB*, bronchiole, ending in a terminal bronchiole, from which are derived the infundibulum, *I*, the atrium, *A*, and the pulmonary alveoli, *PA*. In the center of the figure a pulmonary alveolus, *PA*, is seen in transection; many similar ones are shown. Hematein and eosin. Photo. $\times 45$.

The **terminal bronchiole** is lined by flattened non-ciliated epithelium which rests upon a thin fibro-muscular coat, the continuation of the mucous membrane of the bronchioles. The muscle still forms an almost complete though very thin investment of circular fibres; the muscle fibres, however, are not continued into the wall

of the pulmonary air sacs. The elastic fibres, derived from the elastic layer of the bronchioles, pass over to the alveolar walls in which they form a delicate network.

The terminal bronchioles are short branching tubules leading to broader spaces, the *alveolar ducts* (*infundibula* of Schultze),

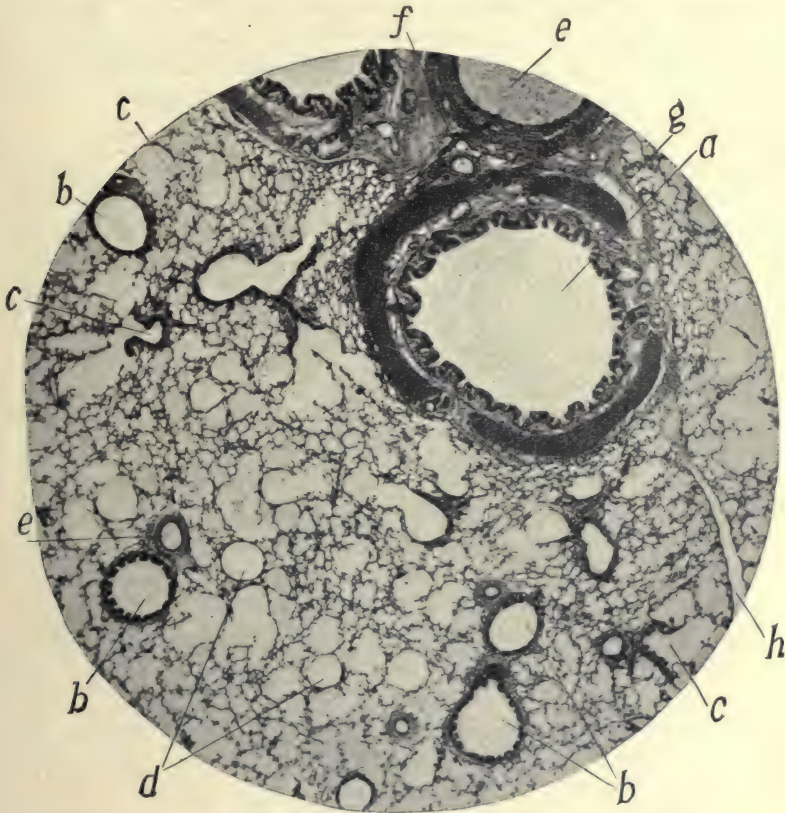


FIG. 203.—FROM A SECTION OF A CHILD'S LUNG.

a, a small bronchus; *b*, bronchioles; *c*, bronchioles ending in terminal bronchioles, infundibuli, etc.; *d*, terminal bronchioles in transection, they have a more regular contour and thicker wall than the alveoli; *e*, pulmonary arteries; *f*, a bronchial artery; *g*, a bronchial vein; *h*, interlobular fibrous septum. Hematein and eosin. Photo. $\times 62$.

which are surrounded by pulmonary alveoli or air saccules. According to W. S. Miller* the alveolar duct is divisible into a main vestibular space and several secondary spaces, the *atria*, which are

* Arch. f. Anat., 1900.

surrounded by the pulmonary *alveoli*. Neither the atria nor the alveolar duct possess a true wall; they are surrounded by the open mouths of the pulmonary alveoli and the thin margins of the alveolar walls.

The **pulmonary alveoli** are minute air cells, open toward the alveolar duct, whose extremely thin wall consists of a capillary network, a delicate fibro-elastic reticulum, and a lining epithelium. The alveoli are so densely clustered about the alveolar duct that

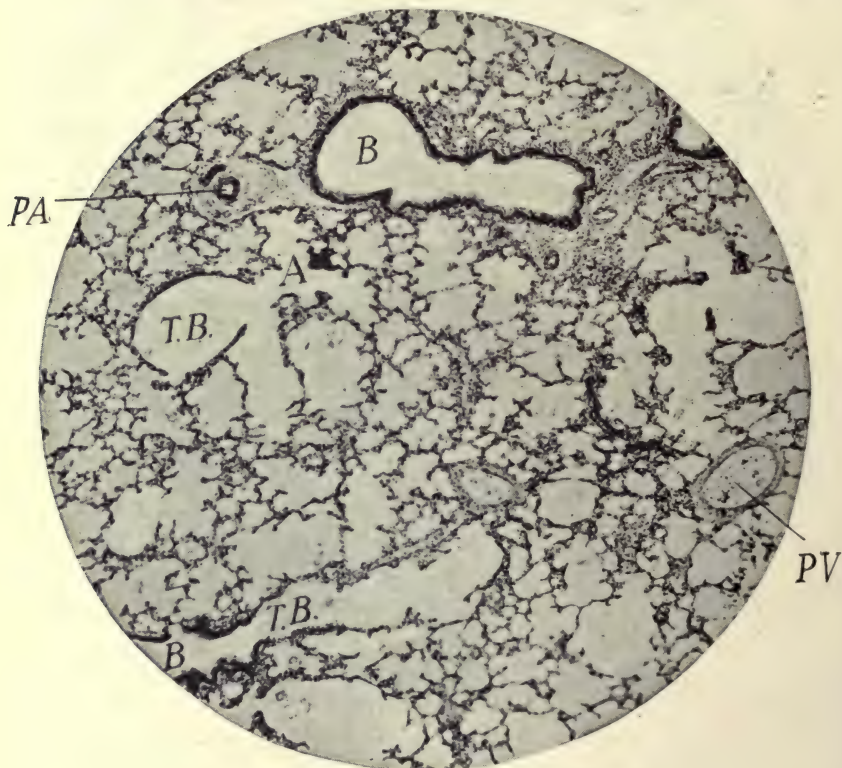


FIG. 204.—FROM A SECTION OF A CHILD'S LUNG.

A, atrium; *B*, bronchioles ending in terminal bronchioles, *T.B.*; *PA*, pulmonary artery; *PV*, pulmonary vein. Hematein and eosin. Photo. $\times 50$.

the capillary plexus, in the form of a reticulated membrane of wide capillary vessels, is exposed to the air of two adjacent alveoli, being separated therefrom only by its own endothelium and the epithelial lining of the alveolus.

The lining epithelium of the alveoli, continuous through the alveolar ducts with that of the terminal bronchioles, consists of flattened or cuboidal cells and broad protoplasmic plates. These cells are narrower and thicker when the lung is collapsed, broader

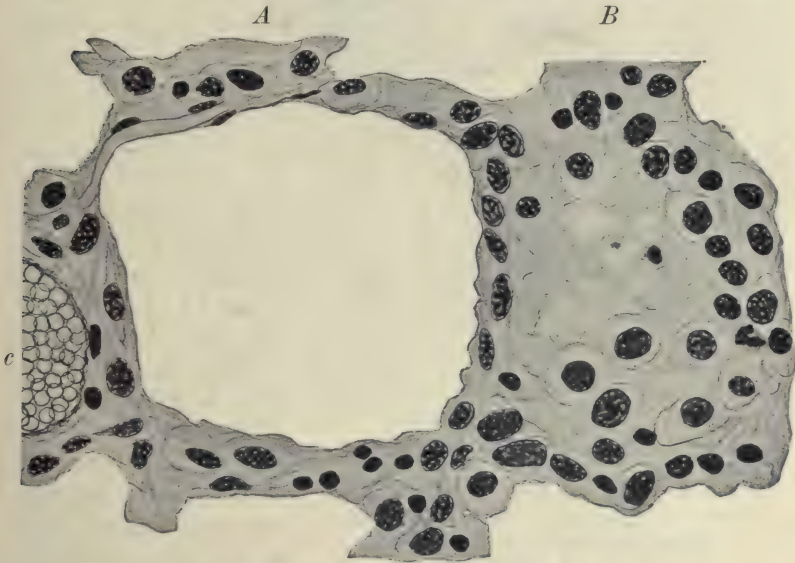


FIG. 205.—TWO ALVEOLI OF A CHILD'S LUNG.

In *A*, the wall is cut across and viewed in profile; *B*, a tangential section showing the cup-shaped bottom of the alveolus and the pulmonary epithelium in surface view; *c*, a pulmonary venule. Hematein and eosin. $\times 640$.

and thinner when it is fully expanded. The completely expanded alveolus in full inspiration is two to three times the size of the collapsed or retracted alveolus of full expiration (Kölliker). The elastic fibres of the alveolar wall form a delicate net among the capillaries; in the meshes of this net a few white fibres are found.

THE PLEURA.—The pleura is a serous membrane whose visceral layer (pleura pulmonalis) envelops the lung, and whose parietal layer (pleura costalis, diaphragmatis, et mediastinalis) lines the thoracic cavity.

The surface of the pleura is clothed with a layer of endothelium which rests upon a "subserous" layer of connective tissue. The endothelium contains frequent stomata which in the costal pleura are only present over the intercostal spaces. The con-

nective tissue contains an abundant network of elastic fibres. It is loosely attached to the chest wall but is more firmly united to the pulmonary tissue.

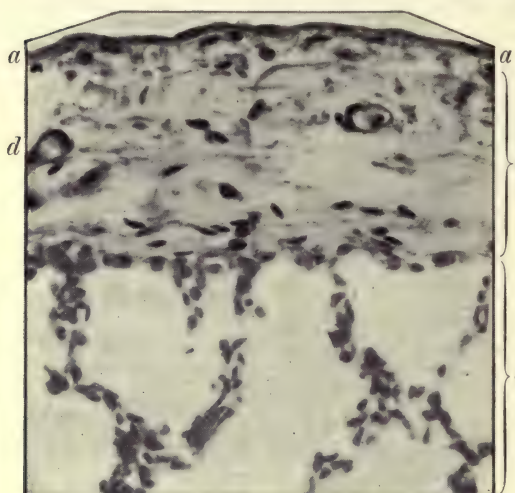


FIG. 206.—TRANSECTION OF THE PLEURA OF AN INFANT.

a-a, layer of endothelium; *b*, subendothelial connective tissue; *c*, pulmonary alveoli; *d*, a small blood vessel. Hematein and eosin. Photo. $\times 470$.

The pleura contains many small blood vessels and an abundant plexus of blood and lymphatic capillaries. Its non-medullated nerve fibres are mostly supplied to the walls of the blood vessels; some, however, terminate in Pacinian corpuscles and in fine sensory terminal branches.

THE LOBULE OF THE LUNG.

—If carefully examined, the surface of the pulmonary pleura presents minute polygonal areas, the bases of the *anatomical*

lobules, whose borders mark the attachment of fine bands of *interlobular connective tissue*. In microscopical preparations still

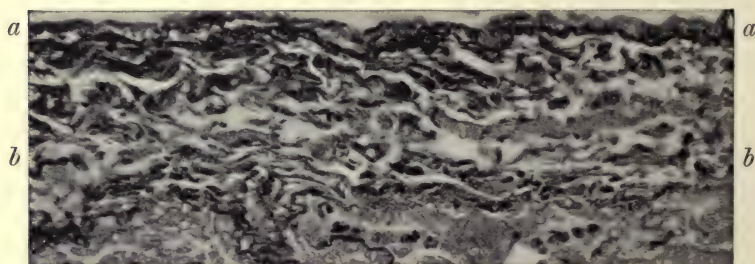


FIG. 207.—FROM A SECTION OF THE PLEURA OF MAN.

The elastic tissue appears black. *a-a*, endothelial surface; *b-b*, subendothelial connective tissue. Weigert's elastic tissue stain, hematein and picro-fuchsin. $\times 110$.

finer bands may be found, which traverse the pulmonary tissue in the direction of the root of the lung, and which partially outline minute conical areas, the true *pulmonary lobules*, whose bases

are directed toward the pleura, and their apices toward the root of the lung. In many of the lower mammals these lobules are more distinctly outlined by interlobular connective tissue than is the case in man.

At its apex a small bronchiole enters the pulmonary lobule and divides into its terminal bronchioles. At the same point a terminal branch of the pulmonary artery enters with the bronchiole and supplies the anastomosing capillary plexus in the alveolar walls. Branches of the bronchial artery do not supply any of the intra-lobular structures, and the pulmonary veins which return the blood from the alveolar capillaries arise at the periphery of the lobule and immediately enter the interlobular connective tissue.

The interlobular connective tissue contains the smaller branches of the pulmonary veins, the lymphatics returning from the pleura, and the non-medullated nerve trunks which are destined for the supply of the pleura and the intralobular pulmonary tissue.

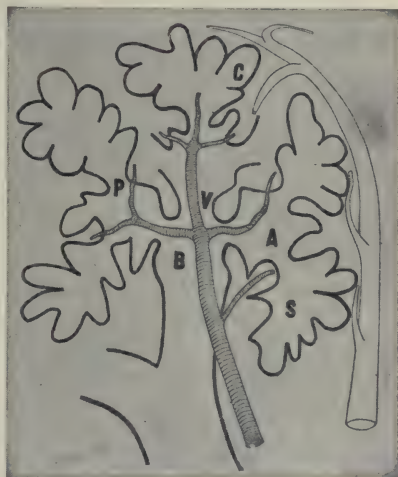


FIG. 208.—DIAGRAM OF A LOBULE OF THE LUNG.

A, atrium; *B*, terminal bronchiole; *C*, pulmonary alveolus; *P*, alveolar duct; *S*, air sac; *V*, infundibulum. The artery is striped, the vein open. (After Miller.)

BLOOD SUPPLY OF THE LUNGS.—The blood supply of the lungs is derived from two distinct sources, the pulmonary arteries and the bronchial arteries. The former is destined chiefly for aëration in the capillaries of the alveolar walls, the latter for the nutrition of the bronchial walls.

The **pulmonary artery** enters at the hilum in company with the vein and the bronchus. It follows the bronchus throughout its course and gives an arterial branch to each of its subdivisions. The large arteries nearly equal in size the bronchus in relation to which they lie, but the smaller branches are not more than one-fourth to one-fifth the diameter of their bronchus. Throughout their course the branches of the pulmonary arteries lie *on* the wall

of the bronchi, viz., in the outer fibrous coat or attached thereto by a broad band of fibrous tissue. Moreover each bronchus is accompanied by only one branch of the pulmonary artery and receives no capillaries from it.

At the apex of the pulmonary lobule the pulmonary artery enters with the bronchiole and immediately breaks into several small twigs—one for each atrium, according to Miller—which sup-

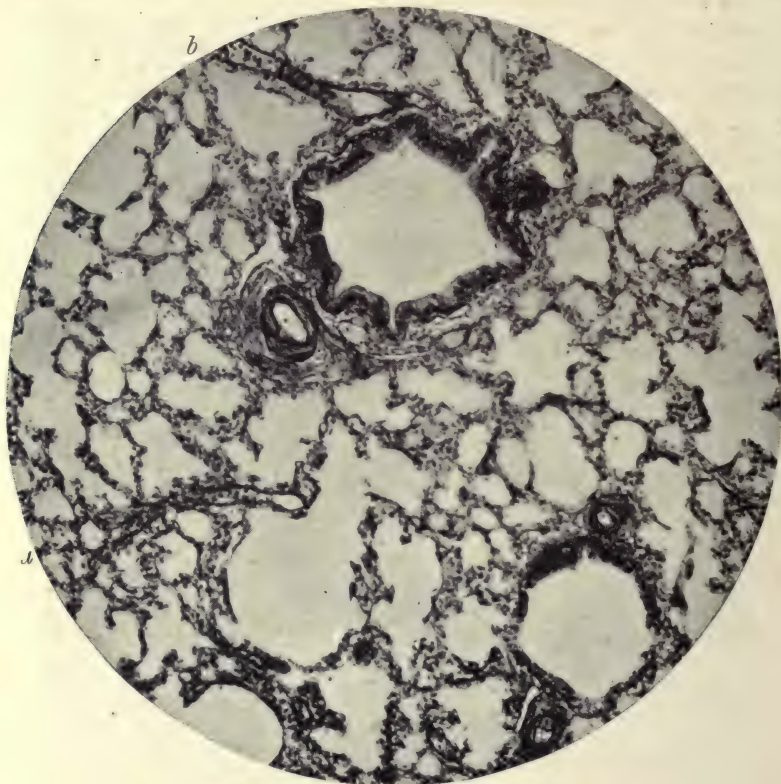


FIG. 209.—FROM THE LUNG OF A CHILD.

At *a*, the origin of a pulmonary venule in the wall of a lobule is shown; at *b*, the pulmonary venule is just coming into relation with the bronchiole. Hematein, Weigert's elastic stain, and picro-fuchsin. Photo. $\times 105$.

ply the capillary networks in the walls of the alveolar ducts and alveoli. The pulmonary capillaries form an exceedingly dense net of anastomosing vessels in the walls of the alveoli, the meshes of the capillary net being frequently, in the deeper portions of the

lung, of less diameter than the vessel itself. At the periphery of the lobule the capillaries converge to form several venules which unite to form larger veins in the interlobular tissue. These veins pursue an independent course and are always found at a consider-

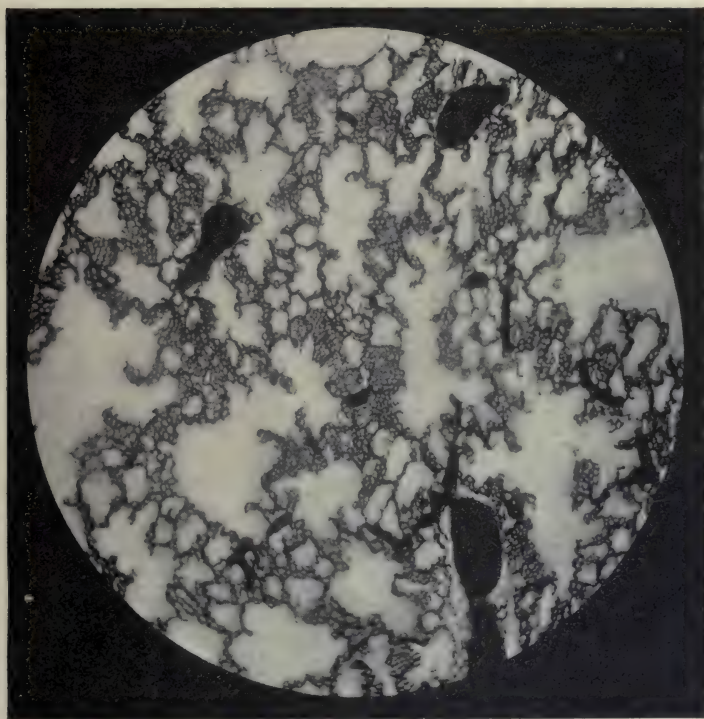


FIG. 210.—FROM THE LUNG OF A DOG WHOSE BLOOD-VESSELS HAD BEEN INJECTED WITH A GELATINOUS MASS, AND APPEAR BLACK.

The outlines of the pulmonary alveoli and infundibula are well shown. Many of the alveoli have been cut tangentially and present a surface view of the capillary network; in others the alveolar wall is cut across and is seen in profile. $\times 125$.

able distance from the bronchioles and lobular branches of the pulmonary artery.

The smaller branches of the pulmonary artery near the surface of the lung give arterial twigs to the adjacent portions of the pleura. From the capillaries of the pleura minute venules enter the interlobular tissue and join the interlobular veins.

The **interlobular veins** (*pulmonary veins*) follow the fibrous septa toward the hilum. They soon come into relation with the

bronchi and are then found on that side of the bronchus opposite the pulmonary artery. The vein, like the artery, lies outside of the bronchial wall in the adjacent fibrous tissue. It is, as a rule, only those bronchi whose wall contains cartilage plates which are in relation with both pulmonary artery and vein; the smaller bronchioles are usually accompanied by the artery only. Those veins

which accompany the bronchi receive smaller branches from the bronchial wall and by union with their fellows form larger and larger vessels which finally make their exit as the pulmonary veins and pass to the left auricle of the heart.

The bronchial arteries also follow the bronchial tubes in all their ramifications. The larger branches are found in the outer fibrous coat near the cartilages, the smaller ones lie in the sub-

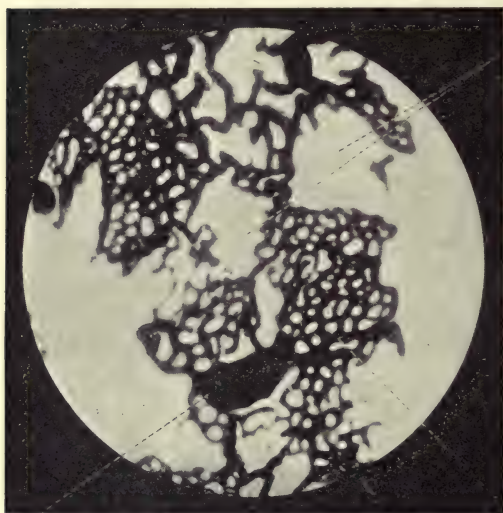


FIG. 211.—FROM THE CENTRAL PORTION OF THE PRECEDING FIGURE.

a, two pulmonary alveoli in transection; *b*, tangential section showing the bottom of an alveolus; *c*, a minute pulmonary venule. Photo. $\times 500$.

mucous and mucous coats. In contradistinction to the pulmonary vessels the bronchial arteries are found *in* the wall of the bronchi, not outside of the bronchial wall. They supply capillaries to all of the tissues of the bronchi. The bronchial capillaries reunite to form small venules whose course differs with the size of the tube. In the terminal bronchioles these venules pass directly to the interlobular veins, and, according to Miller, the pulmonary veins receive a similar acquisition at each division of the bronchi. In the larger bronchi, however, the venules unite within the bronchial wall to form the radicals of the bronchial vein which, lying in the fibrous tissue of the bronchial walls, retrace the course of the bronchi to the hilum, where they make their exit as the bronchial

veins and join the azygos veins. Thus, only the walls of the larger bronchial tubes are supplied with bronchial blood, and, according to Schaffer, a few branches at the root of the lung are also distributed to the adjacent pleura. Many of the bronchioles, the terminal bronchioles, and also the alveolar ducts, pulmonary alveoli, and the pleura all receive their nutrition from the pulmonary arteries. Finally it may be said that there are no anastomoses between the pulmonary arteries and veins except among the capillaries of the alveolar walls.

LYMPHATICS.—The pulmonary lymphatics form a plexus in the walls of the bronchi and bronchioles, the smaller vessels being found in the mucous membrane, the larger in the outer fibrous coat. Branches from this plexus frequently anastomose with perivascular lymphatic vessels about the branches of the pulmonary artery and veins. A close network of lymphatic vessels is also found in the pleura, its efferent vessels passing into the interlobular tissue to join those vessels which accompany the veins. The pulmonary lymphatics are supplied with frequent valves and numerous anastomoses.

The lymphatic vessels of the bronchi are connected with larger lymphatic vessels of the outer fibrous coat and with the lymphatic nodules in the walls of the larger tubes. Many of the larger vessels in the outer fibrous coat of the bronchi, and also those which accompany the pulmonary artery, enter those lymphatic glands which are in relation with the bronchial walls at the root of the lungs. The pleural lymphatic plexus and the vessels accompanying the pulmonary veins, after pursuing much of their course through the interlobular connective tissue in company with the pulmonary veins, also open into the bronchial lymphatic glands. Much pigment is conveyed through these vessels and is deposited in (*a*) the interlobulär connective tissue, (*b*) the fibrous tissue about the pulmonary arteries, and most abundantly in (*c*) the bronchial lymphatic nodules and glands.

NERVE SUPPLY.—The nerves of the lungs are derived from the anterior and posterior pulmonary plexuses of the sympathetic system. They are distributed to the walls of the blood vessels, where they form a delicate plexus with terminal fibrils among the smooth muscle fibres, and to the walls of the bronchial tubes. Small nerve trunks, with which many minute ganglia are connected, occur in large numbers in the outer fibrous coat of the bronchi.

From these nerve trunks and ganglia fibrils are distributed to the bronchial mucous membrane, in which they supply the muscularis mucosæ, and form a terminal plexus beneath the epithelial coat. According to Berkley* these fibres are continued to the terminal bronchioles, whence they form a delicate plexus within the lobule in the interalveolar walls (Wolff,† Cuccati ‡).

* Johns Hop. Hosp. Rep., 1894.

† Arch. f. Anat., 1902.

‡ Internat. Monatschr. f. Anat. u. Physiol., 1888: also *ibid.*, 1889.

CHAPTER XV

THE DIGESTIVE SYSTEM

THE digestive system includes the cavities of the mouth, pharynx, esophagus, stomach, and intestines, together with the accessory glands—the salivary glands, pancreas, and liver. These latter organs will form the subjects of subsequent chapters.

THE MOUTH

The walls of the oral cavity comprise a mucous membrane, a submucous layer of connective tissue, and a muscular or bony paries.

The mucous membrane (mucosa) is clothed with a layer of stratified epithelium which presents, at the margin of the lips, a gradual transition to the epidermis of the skin, and at the fauces is continuous with the lining epithelium of the faucial isthmus and the pharynx.

The tunica propia (corium, stratum proprium) upon which the epithelium rests, consists of dense areolar tissue, the superficial portion of which specially abounds in elastic fibres. This portion of the corium consists of rather delicate connective tissue bundles which at frequent intervals are prolonged into the epithelial coat in the form of minute conical papillæ, similar to those of the skin, whose height varies with the location. The tallest papillæ are found on the gums and at the margins of the lips, the lowest on the inner surface of the cheeks and the soft palate.

The papillary layer of the corium contains a plexus of capillary blood vessels which is connected with a network of small arteries and veins in the deeper part of the tunica propria.

The submucosa consists of looser connective tissue which blends insensibly with that of the mucosa, and unites the mucous membrane to the subjacent muscles and bones forming the wall of the oral cavity. In most portions the buccal mucous membrane is but loosely connected with the underlying parts, but in the hard palate and the gums this union is very firm.

Lymphoid tissue occurs in considerable abundance in the oral mucous membrane. Areas of diffuse lymphoid tissue are of frequent occurrence and small lymphatic nodules are occasionally



FIG. 212.—FROM A SECTION THROUGH THE LIP OF AN INFANT.

a, cutaneous surface; *b*, epithelium of the oral mucosa; *c*, layer of striated muscle; *d*, layer of mucous glands. Hematein and eosin. Photo. $\times 10$.

found. The lymphatic vessels form a plexus in the tunica propria, which empties into larger vessels in the submucosa.

Secreting glands occur in considerable abundance in all portions of the buccal mucous membrane except that covering the gums. The glands are of the tubulo-acinar type and produce either a pure mucous secretion or, in the case of the larger ones, a mixed mucous and serous secretion. The ducts of the glands are lined by columnar cells which, near the mouth of the duct, offer a gradual transition to the stratified epithelium of the mucosa. The

glandular epithelial cells of the secreting portions become swollen and clear *after* a period of rest, but are shrunken and present a faint cytoplasmic reticulum *after* activity. The different glands of the same region, and even different cells in the same gland, often exhibit various stages of secretory activity. The fundus of the secreting glands frequently extends into the loose connective tissue of the submucosa. At the margin of the lips and more rarely in the neighboring portions of the buccal mucous membrane are small sebaceous glands which open directly upon the free surface.

THE TEETH

Each tooth rests in a bony socket in the alveolar process of the maxillary bone, and is also held in place by the periosteum of the alveolar sac and the adjacent portion of the gum. The tooth is divisible into a free portion or *crown*, and a concealed portion or *root* which usually consists of one to three *fangs*. The slightly constricted border between the root and the crown, which is surrounded by the soft tissues of the gum, is known as the *neck* of the tooth.

The tooth also contains a superficial calcareous portion and a central medulla, the *pulp cavity*, which occupies the axis of the tooth and which contains a peculiar embryonic type of connective tissue, the *dental pulp*. At the tip of each fang a narrow canal penetrates the wall of the tooth and permits the entrance of the nerves and blood vessels which supply the pulp cavity.

The calcareous wall of the tooth is formed by three distinct tissues: 1, *dentine*; 2, *enamel*; 3, *cementum*. The dentine incloses the entire pulp cavity and is in turn covered by the enamel and cementum, the enamel forming the superficial layer of the crown, the cementum that of the root of the tooth.

The **dental pulp** is an embryonic type of connective tissue which is rich in branching stellate cells and poor in fibres. It contains no elastic fibrils, and the delicate white fibres instead of forming bundles are arranged in an interlacing network, the fine fibrils of which are in intimate relation with the connective tissue cells. The stellate connective tissue cells are scattered throughout the entire pulp, but at the periphery of the cavity are closely crowded and are much enlarged. These peripheral cells form a layer of *odontoblasts* which is in contact with the dentine.

The odontoblasts are cylindrical branched connective tissue cells whose long axis is perpendicular to the surface of the adja-

cent dentine. From their apex a delicate process is sent into the dentinal canals, in which they frequently extend all the way through the dentine. Lateral processes from the cell bodies of

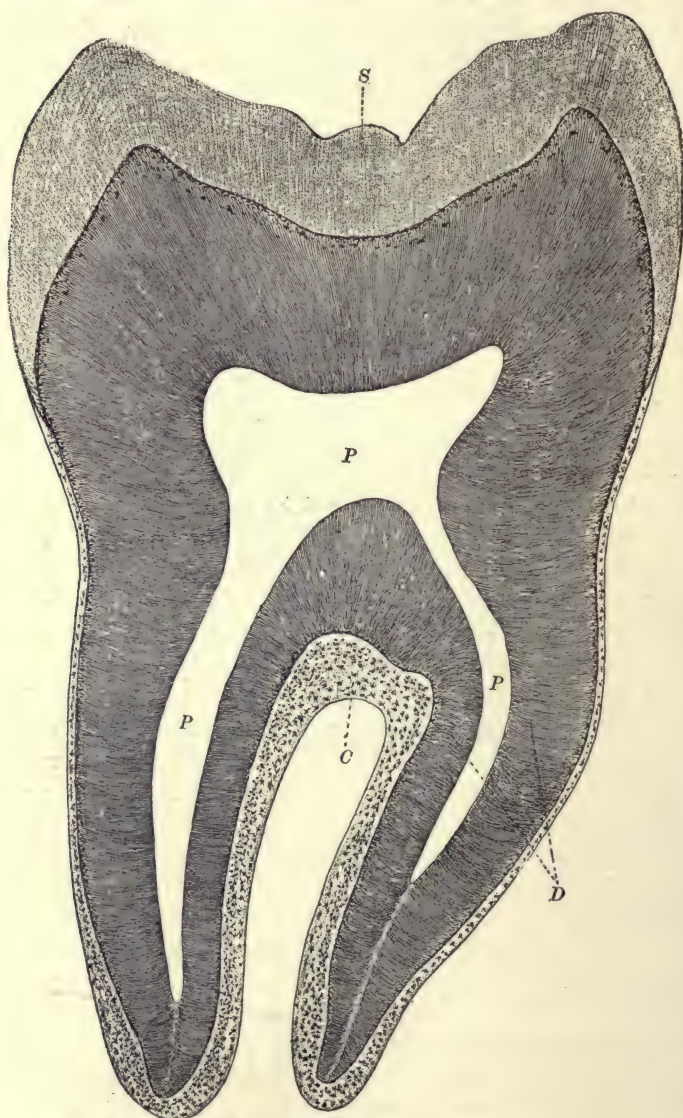


FIG. 213.—AXIAL SECTION OF A HUMAN MOLAR TOOTH.

C, cementum; *D*, dentine; *P*, pulp cavity; *S*, enamel. $\times 8$. (After Sobotta.)

the odontoblasts interlace with each other and firmly unite the cells into a membranous layer. Other processes are given off from the base of these cells and intermingle with the fibres of the pulp, so that if this tissue is forcibly separated from the dentine the odontoblasts remain adherent to the connective tissue of the pulp. The nuclei of the odontoblasts are found near their inner or basal extremity. Their cytoplasm is of considerable extent as compared with that of the other connective tissue cells of the pulp.

The dental pulp is richly supplied with blood vessels, derived from a nutrient artery which enters through the root canal, its branches forming a network of minute arterioles and capillary vessels in the center of the pulp cavity, and a peripheral close-meshed capillary network which is in close relation with the layer of odontoblasts. There are no lymphatic vessels in the tissue of the dental pulp.

A rich nerve supply is derived from fine branches which also enter by the root canal. Most of the nerve fibres lose their myelin sheaths soon after they enter the pulp. They form a primary plexus in the connective tissue from which

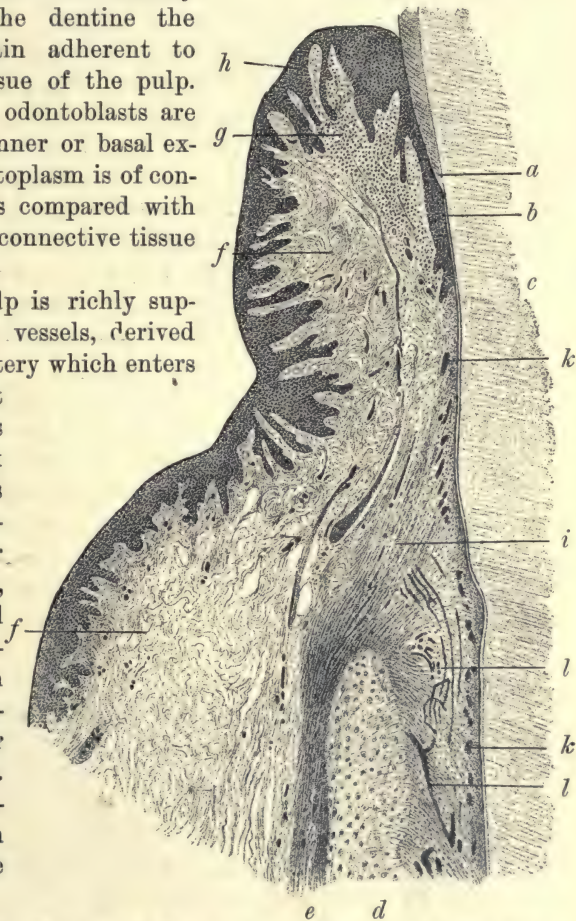


FIG. 214.—FROM A LONGITUDINAL SECTION OF THE NECK OF A CHILD'S TOOTH AND THE ADJACENT ALVEOLUS.

a, enamel; *b*, cementum; *c*, dentine; *d*, bone; *e*, periosteum; *f*, corium; *g*, lymphoid tissue; *h*, stratified epithelium of the gum; *i*, circular dental ligament; *k*, epithelial remnants; *l*, blood vessels. $\times 25$. (After Kölliker.)

fine fibres pass to the periphery and form a network of terminal fibrils which end among the odontoblasts. Boll,* though suggesting that the terminal nerve fibrils enter the dentinal canals, was yet unable to demonstrate the theory. More recent observers (Retzius,† *et als.*) have likewise been unable to recognize any nerve fibrils beyond the layer of odontoblasts. Boll's theory of nerve fibrils within the dentinal canals, therefore, still lacks satisfactory confirmation.

Dentine.—The dentine surrounds the entire pulp cavity except at the opening of the root canal. It is a fine calcareous substance which resembles bone in that it consists of a fibrous matrix and is infiltrated with lime salts. The matrix is a fine fibrous network of dense connective tissue, the majority of whose fibres are disposed in a longitudinal direction. The meshes of the matrix are almost completely filled by a deposit of calcareous salts which gives the dentine its bony consistence.

Here and there, especially toward its peripheral border and near the apex of the tooth, the dentinal matrix fails to become calcified. Such uncalcified areas, *interglobular spaces*, are encroached upon by the rounded or globular margins of the adjacent calcified matrix which forms the so-called dental globules.

The dentine is everywhere permeated by a system of canaliculi, the *dentinal tubules* or canals, which extend in a radial manner from the pulp cavity outward to the cementum and enamel.

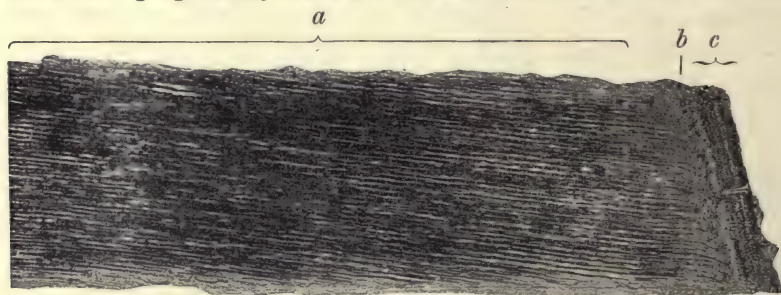


FIG. 215.—FROM A SECTION OF A HUMAN TOOTH WHICH HAD BEEN GROUND TO EXTREME THINNESS.

a, dentine; b, granular layer of Thomes; c, enamel. Photo. $\times 150$.

Their course is characteristically curved, resembling the letter *f*. The cavity of the dentinal tubules is partially occupied by the dentinal processes of the odontoblasts, an arrangement which may

* Arch. f. mik. Anat., 1868.

† Biol. Untersuch., 1894, N. F., vol. vi.

be compared to the bone corpuscles and canaliculi of bone. At their inner extremity the dentinal tubules are 2 to 4 μ in diameter, but they taper very gradually, especially in the outer portion of their course, where they finally reach a diameter of no more than 0.5 to 1 μ .

Throughout their course the dentinal tubules give off very fine lateral twigs, which at first leave the parent tubule nearly at right angles, but later are slightly inclined outward. At their distal end most of the dentinal tubules divide into a group of terminal branches, some of the arborizations being very extensive, others consisting of but two or three subdivisions. The coarser branches are frequently looped, the distal end of the loop often anastomosing with adjacent tubules. In their course through the dentine those canaliculi which enter the interglobular spaces are continued through these spaces without interruption.

The walls of the dentinal tubules are formed by extremely dense calcareous *dentinal sheaths* which are very resistant to the action of acids. The curvatures in the course of the dentinal tubules, occurring with extreme regularity, give rise to certain parallel lines in the substance of the dentine which follow the contour of the dentinal surface. These are known as the *incremental lines* of *Schreger*.

The superficial portion of the dentine is formed by the **granular layer of Thomes**, in which there are no dentinal tubules, but instead there are in this layer numerous small interglobular spaces from which minute canaliculi radiate in various directions. Many of these canaliculi are connected, on the one hand with the dentinal tubules, and on the other with the canaliculi and bony lacunæ of the cementum. The canaliculi of the granular layer are readily distinguished from the adjacent dentinal tubules by the extreme irregularity of their course, which contrasts sharply with the straight or regularly curved course of the dentinal tubules.

The granular layer is relatively thick in the root of the tooth, but becomes much thinner toward the neck. Beneath the enamel it becomes so thin that toward the apex of the tooth it is scarcely demonstrable. At this point, also, occasional dentinal tubules are continued for a short distance into the enamel, though this condition is more characteristically developed in some of the lower mammals (e. g., *Rodentia*) than in man.

Enamel.—The enamel, which covers the exposed crown of the tooth, is the hardest tissue of the body. It consists of many cal-

careous cylinders, the *enamel prisms*. These radiate outward from the dentine and are disposed after the manner of a mosaic. They are firmly united to each other by a very thin layer of calcified



FIG. 216.—ENAMEL
PRISMS IN TRAN-
SECTION.

From the tooth of
a calf. $\times 350$. (Af-
ter Kölliker.)

cement substance. Strangely enough the enamel prisms are developed from epithelial cells, by which they are apparently deposited as a calcareous cuticular formation, the calcification proceeding from within outward. The uncalcified cytoplasm of the outer portion of these cells becomes highly cornified, so that the free surface of a recently erupted tooth is covered by a thin horny cuticle, the *cuticular membrane* of Nasmyth. The cuticular covering which is thus formed by the horny uncalcified portions of the enamel cells is, however, removed by mechanical

violence in a relatively short time after the final eruption of the tooth.

The enamel prisms are grouped into bundles within which the constituent prisms are parallel. The course of the prism bundles, however, is variable, so that, though following a more or less radial course through the enamel, the prism bundles frequently cross one another at acute angles. In the thicker portions of the enamel this peculiarity gives rise to an apparently laminated condition of this tissue.

Ground sections of dried tooth show brownish lines having a general radial direction, but which are somewhat inclined toward the apex of the tooth. These *lines of Retzius* are explained by von Ebner as being the result of air-filled fissures in the dried enamel. They are also said to be the result of the wavy direction of the enamel prisms.

Cementum.—The dental cement, *crusta petrosa*, is a thin layer of bony tissue which invests the root of the tooth. It forms a very thin layer at the neck of the tooth, but gradually increases in thickness as it approaches the tip of the fang.

The cementum consists of parallel layers of bony lamellæ between which many lacunæ with their bone corpuscles are included. Bone canaliculi radiate from the lacunæ and frequently open into the interglobular spaces of the granular layer. There are no Haversian systems in the cementum, but the thicker portions are frequently penetrated by vascular canals which, like Volkmann's canals, are not accompanied by concentric lamellæ. The cement-

um is firmly united to the granular layer of the dentine, the matrix of the two tissues being continuous.

The cementum is invested with a periosteal coat, the periodontium, alveolar periosteum, or *root membrane*, of dense fibrous tissue which, at the neck of the tooth, unites with the dense connective tissue of the gum to form an annular thickening of very

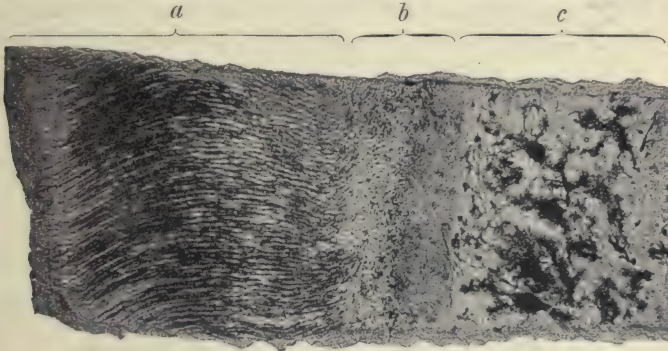


FIG. 217.—FROM A SECTION OF A HUMAN TOOTH WHICH HAD BEEN GROUND TO EXTREME THINNESS.

a, dentine; b, granular layer of Thomes; c, cementum. Photo. $\times 140$.

dense fibrous tissue which encircles the tooth and is known as the *circular dental ligament*. The root membrane contains no elastic fibres, but sends considerable numbers of slender white fibrous bands (Sharpey's fibres) into the cementum.

DEVELOPMENT OF THE TEETH

The teeth arise partly from the epithelium of the oral cavity and partly from the connective tissue of the alveolar processes. In the seventh week of fetal life there appears upon the surface of the maxillary ridges a thickening of the epithelium which grows into the subjacent connective tissue in the form of a longitudinal ridge or shelf, the *dental ridge*, whose position is indicated by a *dental groove* which indents the epithelial surface.

The dental ridge forms the earliest anlage of the enamel, and at this early stage it shows no indication of the future subdivisions which correspond to the several temporary teeth. On its inner side is a similar ingrowth of epithelial cells which is destined to form the vallum between the lips and the alveolar processes.

At the beginning of the third month the dental ridge shows upon its deep margin slight indentations, one for each of the tem-

porary teeth, which are produced by a growth and thickening of the mesenchymal connective tissue cells at the site of each tooth germ. This thickening of the connective tissue forms the anlage

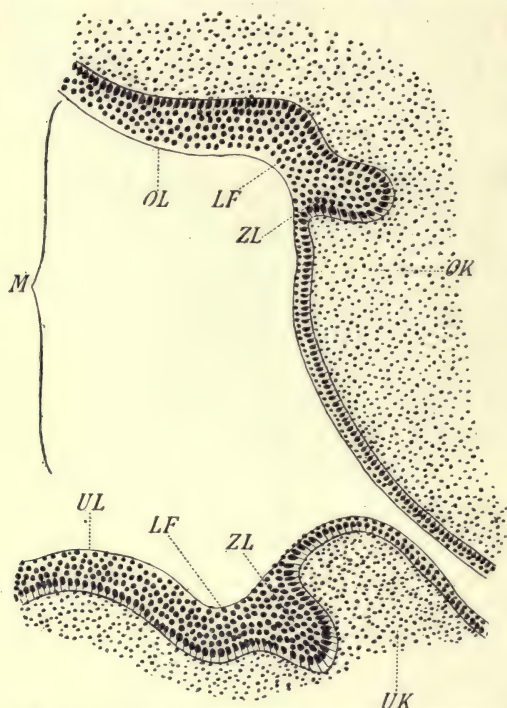


FIG. 218.—DEVELOPING TOOTH FROM A HUMAN EMBRYO
17 MM. LONG.

LF, dental groove; M, oral cavity; OK, mesoblast of upper jaw; OL, epithelium of the primitive upper lip, and UL, of the lower lip; ZL, dental ridge. $\times 120$. (After C. Rösé.)

of the *dental papilla*. That portion of the dental ridge which spreads out laterally to cover the dental papilla of each tooth forms its *enamel germ*, from which the dental enamel is eventually produced. Further development of the enamel germ and dental papilla causes the former to surround the papilla like a cap.

During the third month of fetal life the anlages of all the primitive teeth are formed in the above manner. At about the same time, also, a lateral growth from the lingual side of the thin portion of the dental ridge which still connects the enamel germs with the oral epithelium, forms the

anlages of the permanent teeth. The molars arise at a later period and in a similar manner by a dorsal extension of the dental ridge which grows backward through the connective tissue of the alveolar process as a solid cell column from which the enamel germs are formed and into which the dental papillæ grow.

Further development of the dental anlage includes the differentiation of the enamel germ on the one hand and of the dental papilla on the other. From the former the enamel and the cuticular membrane arise; the latter produces the dental pulp and the dentine.

The Enamel Germ.—The enamel germ or *enamel organ* soon differentiates into three layers: 1, an *inner enamel epithelium* which forms the enamel prisms; 2, an *outer enamel epithelium* which lines the dental sac; and 3, an intervening *enamel pulp*.

The Inner Enamel Epithelium.—The innermost cells of the enamel organ, viz., those which rest directly upon the dental papilla, soon become elongated and attain a cylindrical form. A cuticular border appears upon the inner extremities, and as the

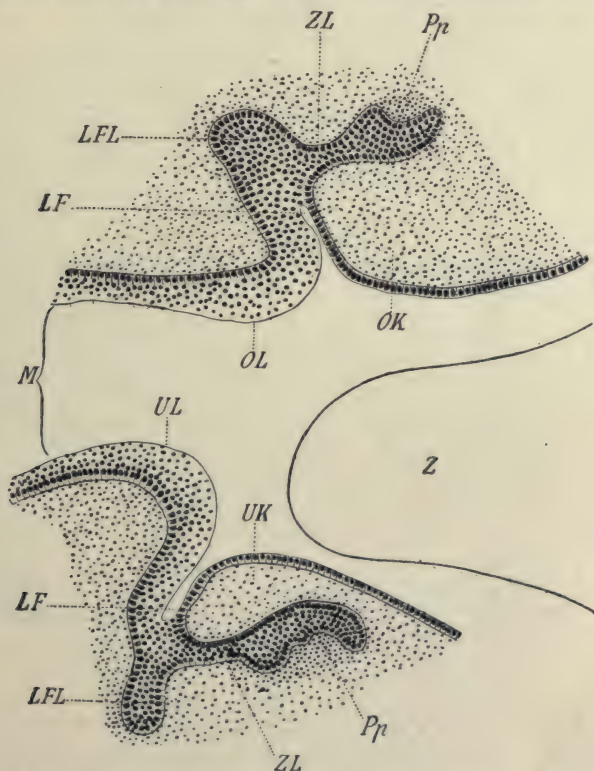


FIG. 219.—DENTAL ANLAGES FROM A HUMAN FETUS 40 MM. LONG.

Letters as in the preceding figure. *LFL*, anlage of the groove between the lip and the mandibular process; *Pr*, dental papilla; *Z*, outline of the margin of the tongue. $\times 60$. (After C. Röse.)

calcareous substance of the enamel begins to be deposited fine processes are seen extending inward from the extremities of the enamel cells, *Thomes' processes*. It is around these processes that the permanent enamel is deposited to form the enamel prisms.

The deposit of lime salts by the cylindrical cells of the inner enamel layer, *adamantoblasts*, occurs earliest at the apex of the dental germ. Thus, it is the enamel of the face of the tooth crown



FIG. 220.—DEVELOPING TOOTH FROM A HUMAN FETUS 30 CM. LONG.

D, dentine; *K*, bone of the jaw; *RM*, Malpighian layer of the oral mucosa; *S*, enamel organ; *SK*², enamel anlage of the permanent tooth; *VB*, epithelial bridge still uniting the anlagen of the temporary and permanent teeth; *ZL*, disintegrating dental ridge. $\times 30$. (After C. Röse.)

which is first formed, and this is therefore its thickest portion. The enamel on the sides of the tooth crown appears later and hence it gradually tapers in thickness as it approaches the neck of the tooth, in which latter place the last formed enamel is found.

The nucleated bases of the cylindrical cells of the inner enamel epithelium are also marked by a sharp cuticular margin and rest upon the adjacent cells of the enamel pulp, the innermost cells of which retain a characteristic epithelial appearance. The thin layer formed by the uncalcified bases of the adamantoblasts, which

still cover the free surface of the enamel at the eruption of the tooth, remains as the cuticular membrane of Nasmyth.

The Outer Enamel Epithelium.—The outermost cells of the enamel germ are immediately in contact with the mesenchymal



FIG. 221.—A DEVELOPING TOOTH FROM AN INFANT'S JAW.

a, papilla; *b*, crown; *c*, outer enamel epithelium. Hematein and eosin. Photo. $\times 65$.

connective tissue of the primitive jaw. This connective tissue forms, toward the end of the third month, an investing sheath or

dental sac, which incloses the entire dental germ and finally, by gradually encroaching upon the narrow neck which still connects the enamel germ with the dental ridge, severs the connection of

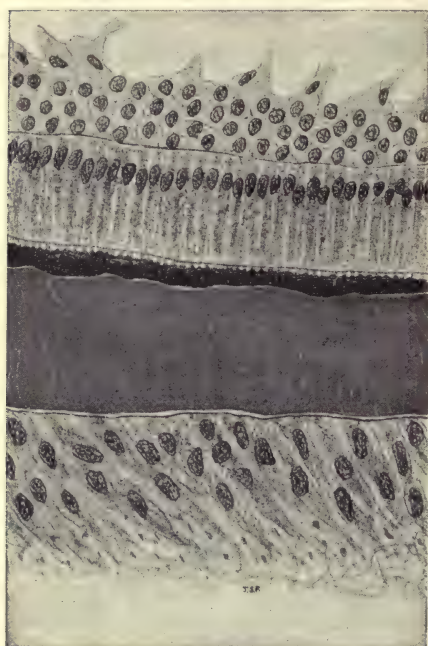


FIG. 222.—A PORTION OF FIG. 221, NEAR THE APEX OF THE DEVELOPING TOOTH.

a, enamel epithelium; *b*, adamantoblasts; *c*, enamel; *d*, dentine; *e*, odontoblasts; *f*, border of the dental pulp. Hematein and eosin. $\times 550$.

these organs so that the primitive tooth lies free within the dental sac. The outer enamel epithelium, which lines all portions of the dental sac except at the base of the dental papilla, forms several layers of flattened epithelial cells. Remnants of this cell layer frequently persist, in relation to the inner margin of the bony alveolus whose wall is produced by intramembranous ossification in the connective tissue surrounding the embryonic dental sac.

The Enamel Pulp.—This structure is produced by a most remarkable differentiation which occurs within the mid-portion of the enamel organ. The epithelial cells of this region, which at first appear to

form a delicate syncytium, become separated by wider and wider intercellular spaces, and are thus drawn out into stellate forms with long anastomosing processes. The resulting cells closely resemble in form the connective tissue cells of embryonic or gelatinous connective tissue. They are, however, inclosed on all sides by the epithelial cells of the inner and outer enamel epithelium and, like other epithelial tissues, are never penetrated by blood vessels.

The enamel pulp appears to serve a purely mechanical function, it being a soft tissue through which the growing tooth readily pushes its way to the surface.

THE DENTAL PAPILLA.—The dental papilla is a connective tissue structure which is invested by and grows into the enamel

organ. Coincident with the appearance of the adamantoblasts in the enamel organ, the superficial cells of the dental papilla become enlarged, elongated, and so arranged as to form a continuous layer of odontoblasts on the surface of the papilla. These cells apparently secrete a thin homogeneous layer, *membrana præformativa* (Raschkow), which serves as a basement membrane upon which the adamantoblasts deposit the enamel prisms; it also forms the anlage of the granular layer of Thomes.

The odontoblasts now form the dentine in a manner entirely analogous to the deposit of bone by the osteoblasts, processes of the odontoblasts being included within the deposit of dentine to form the dentinal fibres. Irregular spaces, occurring in the dentine and granular layer, in which no calcification occurs produce the interglobular spaces.

The central mass of the dental papilla develops the embryonic connective tissue of the tooth pulp. The blood vessels and nerves enter the pulp through the base of the papilla, which thus becomes the anlage of the root canal.

The cementum is formed by intramembranous ossification occurring in the connective tissue which invests the base of the dental papilla and the primitive root of the tooth.

THE TONGUE

The tongue is formed by a reflection of the oral mucous membrane which incloses a mass of muscular tissue. The fibres of this striated muscle are separated into two lateral halves by a median septum of dense connective tissue which extends from the base to the tip of the organ, and is known as the *lingual septum*.

The muscle fibres are disposed in three planes and are so arranged that the bundles cross one another at right angles. They thus form: 1, saggital or vertical fibre bundles which are slightly inclined outward from the septum linguæ and are derived from the lingualis muscle; 2, longitudinal fibres running from the base to the apex of the tongue, which are derived from the lingualis, styloglossus, hyoglossus, genioglossus; 3, transverse or horizontal fibres extending laterally from the septum linguæ, which are also derived from the lingualis muscle.

The interlacing bundles of muscle fibres are embedded in loose areolar and adipose tissue. The muscle fibres are inserted into the corium of the lingual mucous membrane, their sarcolemma being firmly adherent to the connective tissue of the mucosa, which

invests the rounded blunt extremity of the muscle cell. Many of these muscle fibres are branched.

The **mucoous membrane** of the tongue consists of a thick corium, and an epithelial covering. The deeper part of the corium, consisting of loose areolar tissue, is intimately connected with the

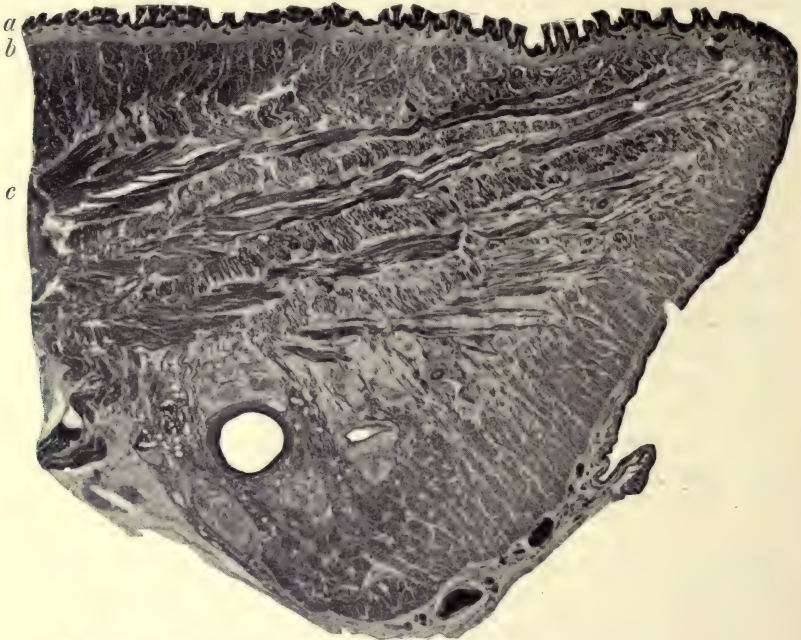


FIG. 223.—ONE LATERAL HALF OF A CORONAL SECTION OF A DOG'S TONGUE.

The dorsal surface presents numerous large filiform papillæ. *a*, lingual papillæ; *b*, corium; *c*, the fibro-muscular substance of the tongue. Hematein and eosin. Photo. $\times 6$.

muscle. The superficial portion of the corium, containing denser areolar tissue, carries upon its surface *papillæ* of unusually large size which project into the epithelial coat. The surface of the larger of these papillæ is not smooth, but is covered with small *secondary papillæ*.

The epithelium of the tongue is of the stratified variety. Upon the under surface and margins of the organ its surface is smooth, but on the dorsum of the tongue the stratified epithelium forms tall projections, which correspond with the papillæ of the corium, and which constitute the so-called *lingual papillæ*. These papillæ are of three varieties: 1, conical or filiform; 2, fungiform; and 3, circumvallate.

The Conical or Filiform Papillæ.—These papillæ consist of flattened and elongated epithelial cells which are often so arranged as to produce a slender conical projection or epithelial tuft of

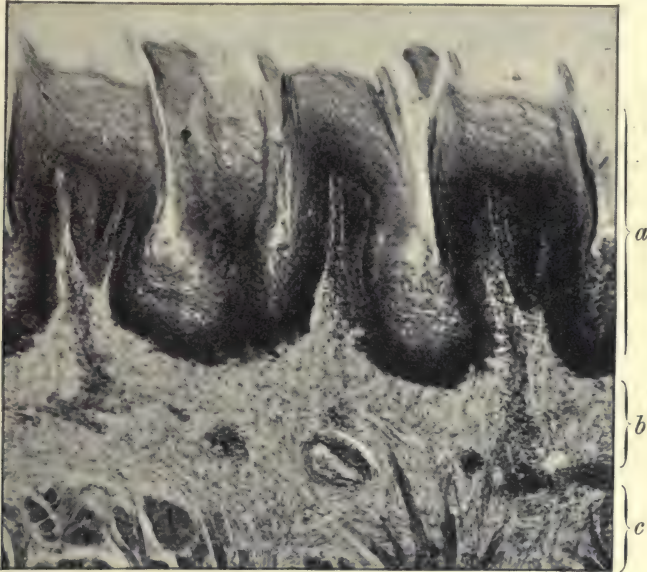


FIG. 224.—FILIFORM PAPILLÆ OF THE DOG'S TONGUE.

a, papillæ; *b*, corium; *c*, insertion of the muscular fibres into the border of the corium.
Hematein and eosin. Photo. $\times 60$.

variable height, which covers the apex of each connective tissue papilla. This type is the most abundant of the three varieties of lingual papillæ; they are found upon all portions of the dorsum of the tongue.

The fungiform papillæ are formed by a large connective tissue papilla or core which projects above the general level of the epithelial surface and is covered by a smooth layer of stratified epithelium in which occasional taste buds are found. This variety, though much less abundant than the former, is still very numerous and may be found upon any or all portions of the dorsum of the tongue, where they are irregularly scattered among the filiform papillæ. The fungiform variety are most abundant near the margin of the tongue on its dorsal surface.

The circumvallate papillæ form a group of from eight to twelve elevations which are situated at the base of the tongue, and are

arranged in the form of an inverted V, the apex being directed toward the larynx. These papillæ are much larger than either of the former varieties. They extend slightly above the general level of the epithelial surface, are of an inverted conical shape, and are covered by a smooth layer of stratified epithelium. Their base is surrounded by a deep circular excavation, lined by an invagination

A

B

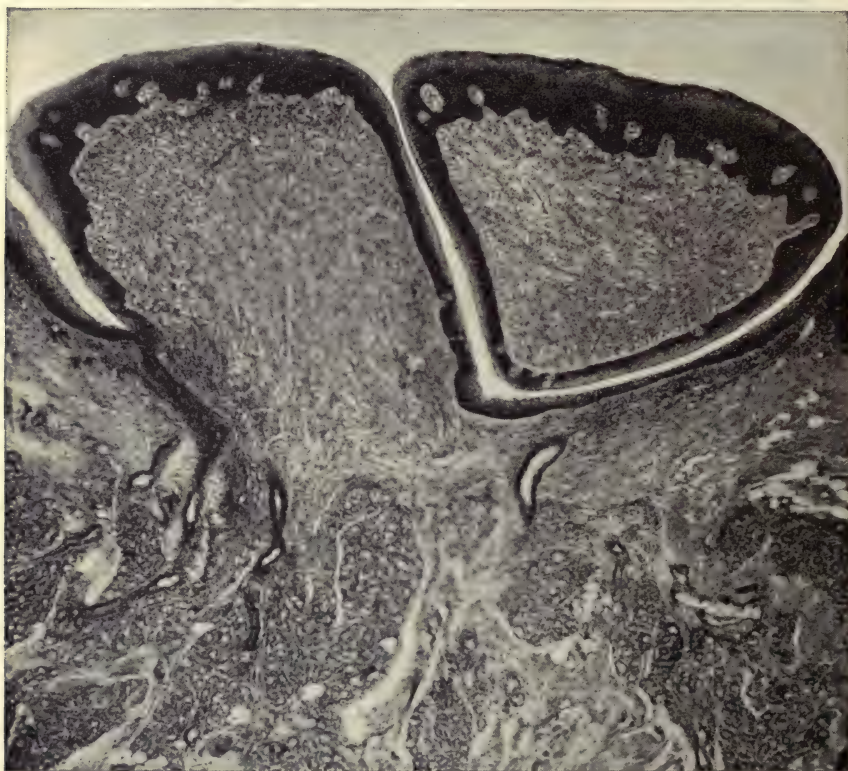


FIG. 225.—CIRCUVALLATE PAPILLÆ OF THE HUMAN TONGUE.

A, axial section; B, section through the side of a papilla. The serous glands of von Ebner occupy the lower portion of the figure. Hematein and eosin. Photo. $\times 40$.

of the layer of stratified epithelium, which thus forms a deep trench or vallum about the base of the papilla.

The epithelium which covers the sides of the circumvallate papillæ, as well as that forming the lateral wall of the vallum, contains large numbers of *taste buds*.* The large central connective

* See Chapter IX.

tissue papilla carries upon its surface many small secondary papillæ of the corium, which project into the epithelial coat of the circumvallate papilla upon its free surface, but are not found upon its lateral margins.

Mucous and serous glands occur in the deeper portion of the corium of the tongue and among its muscle bundles; they open upon its epithelial surface between the papillæ. These glands are most abundant at the base of the organ but are also found along its margins as far forward as the tip, where a pair of small tubulo-acinar mucous glands lie on either side of the median septum and open upon the ventral surface of the tongue; these are the *anterior lingual glands* of Nuhn.* The serous glands of von Ebner are confined to the region of the circumvallate papillæ at the base of the tongue. They pour their secretion into the valium which surrounds the base of the papilla or into the crypts of the lingual tonsil. Other lingual glands, also of the small tubulo-acinar type, occur at various portions of the dorsal surface of the tongue.

The lingual tonsil (Fig. 153, page 157) is a considerable collection of lymphoid nodules which is found at the base of the tongue in and about the median line. These nodules are grouped about a large funnel-shaped crypt, the *foramen cæcum*, which opens at the apex of the V formed by the group of circumvallate papillæ and which in the embryo forms the lingual extremity of the so-called duct of the thyroid gland (*thyreo-glossal duct*). Several smaller crypts are also included in the region of the lingual tonsil.

The lymphoid nodules are embedded in the mucosa or corium of the tongue and are surrounded by mucous glands many of whose ducts penetrate between the nodules to open into the branching crypts. Lymphatic corpuscles, apparently derived from the nodules, infiltrate the surrounding connective tissue and epithelium and find their way into the lumen of the follicular crypts.

In other portions of the lingual mucous membrane diffuse collections of lymphatic corpuscles are of frequent occurrence, and small nodules occur in many parts of the dorsal mucous membrane toward the base of the tongue.

The blood vessels of the tongue are supplied by large arteries which, with the corresponding veins, are embedded in the muscular portion of the organ and supply capillary vessels to this tissue.

* Mannheim, 1845.

From these arteries, also, small arterial branches enter the deeper portion of the corium and form a capillary plexus which supplies the connective tissue and whose terminal ramifications extend to the very apex of the connective tissue papillæ. The blood is returned by veins which pursue a similar course.

The Lymphatics form a superficial set of small vessels and tissue spaces beneath the epithelial layer, which are especially abundant in the region of the lingual tonsil at the base of the tongue. The lymphatic vessels of this superficial plexus frequently encircle the lymphoid nodules. A deeper plexus of lymphatics in the loose connective tissue of the submucosa receives the lymph from the superficial plexus and conveys it by efferent lymphatic vessels to the deep cervical lymphatic glands.

The Nerves of the tongue are derived from the lingual, glossopharyngeal, and chorda tympani. The larger trunks accompany the arteries, lying near the median line on the under surface of the tongue, and are embedded in the connective and adipose tissue between the muscle bundles of this portion of the organ, small *ganglia* occurring along their course. From these nerve trunks, fibres are distributed to the muscular tissue and to the corium. The former terminate in muscle plates in the striated muscle fibres, in the walls of the larger blood vessels to which both sensory and motor fibres are distributed, and in sensory endings in the muscle spindles and connective tissue. The smaller nerves of the corium supply the blood vessels of this tissue and send minute fibrils to the epithelium, which terminate in delicate knobbed extremities between the epithelial cells.

At the base of the tongue small nerve bundles are distributed to the circumvallate papillæ, and form a subepithelial plexus from which fibrils are distributed: 1, to the interior of the taste buds where they end in relation with the gustatory cells, *intragemmal fibres*; 2, to the surface of the taste buds, *perigemmal fibres*; and 3, to the intervening portions of the epithelial layer, where they end between the epithelial cells as in other parts of the tongue, *intergemmal fibres* (Fig. 120, page 125).

CHAPTER XVI

THE DIGESTIVE SYSTEM (*Continued*)

THE ALIMENTARY TRACT

It is convenient to consider collectively under this head the pharynx, esophagus, stomach, and the small and large intestines. This tract forms a continuous tube whose wall has, throughout its entire extent, many common characteristics. Thus the wall in all portions consists of four coats which are respectively known, from within outward, as the mucous, submucous, muscular, and fibro-serous. The three outermost coats are of very similar structure in all portions of the tract.

The Fibro-serous Coat.—In the abdominal cavity the outermost coat is derived from the peritoneum, by which the stomach and intestines are invested. In the upper portion of the tract, pharynx and esophagus, the serous coat is replaced by a layer of areolar connective tissue which usually contains much fat. In the abdomen the homologous subserous connective tissue is covered by a layer of endothelium. The connective tissue of the outer fibro-serous coat contains the larger blood and lymphatic vessels whose branches are distributed to the three inner coats.

The Muscular Coat, situated next within the fibro-serous, is divisible into two layers, an outer longitudinal the direction of whose fibres is parallel to the long axis of the tract, and an inner transverse layer whose fibres are circularly disposed. The two layers are united by a thin septum of areolar connective tissue which serves for the support of the larger blood vessels and lymphatics, whose capillaries are distributed to the muscular coat. This septum also contains a coarse-meshed nerve plexus, consisting of small anastomosing nerve trunks which are composed in large part of non-medullated fibres, at whose intersections are numerous small sympathetic ganglia. This is the nerve *plexus of Auerbach*.

Below the level of the junction of the middle and lower third

of the esophagus, and including the musculature of the stomach and intestines, the muscle is entirely of the non-striated or smooth variety. In the pharynx and upper third of the esophagus, the striated or voluntary type of muscle is exclusively found. In the mid-portion of the esophagus both striated and non-striated muscle occur in varying proportions, occasional striated fibres being found even in the lower third of the organ.

The Submucous Coat consists of loose areolar tissue, and serves for the support of the larger blood and lymphatic vessels which supply this coat and the



FIG. 226.—SURFACE VIEW OF AUERBACH'S INTRA-MUSCULAR NERVE PLEXUS, FROM THE ESOPHAGUS OF A CAT.

Methylen blue. $\times 40$ to 50. (After De Witt.)

mucosa. A second plexus of nerve fibres, similar in structure to the intra-muscular plexus, is found in the deeper layers of the submucosa, and is known as the *plexus of Meissner*. Its nerve trunks and ganglia are somewhat smaller than those of the plexus of Auerbach. The plexus of Meissner supplies the muscular and glandular tissues of the mucous membrane.

The Mucous Membrane or mucosa of the gastro-intestinal tract contains four typical structures, (1) an internal lining epithelium; (2) the muscularis mucosæ which forms the outermost layer; between these is (3) a tunica propria or corium of diffuse lymphoid or areolar tissue, which serves chiefly for the support of (4) the secreting glands.

The muscularis mucosæ usually consists of a double layer of involuntary or smooth muscle, the outer being longitudinally, the inner transversely or circularly disposed. This layer is most highly developed in the esophagus.

The tunica propria consists of loose areolar or reticular tissue whose volume is in inverse proportion to that of the secreting glands. It is most abundant in the esophagus. In the stomach and intestines it is considerably infiltrated by lymphatic corpuscles and often contains diffuse lymphoid tissue. Small lymphatic nodules are also found in the deeper part of this membrane; they

progressively increase in size toward the lower portion of the tract, where they form the solitary follicles of the intestine.

The nature of the lining epithelium and the type of the secreting glands differs in each succeeding portion of the tract, and must therefore, together with the other peculiarities of the several subdivisions of the tract, be separately considered.

THE PHARYNX

The pharynx may be subdivided, upon histological as well as physiological grounds, into (1) an upper respiratory portion, or naso-pharynx, and (2) a lower portion, oro-pharynx and laryngo-pharynx; only the latter of these properly belongs to the alimentary tract. The naso-pharynx has already been described as a part of the respiratory system (see Chapter XIV).

The mucous membrane of the lower portion of the pharynx is lined by stratified squamous epithelium which rests upon a thick corium of areolar tissue. The tunica propria is well supplied with thin-walled blood vessels and lymphatics, and contains many mucus secreting glands of the tubulo-acinar type whose secreting portions lie deeply embedded in the connective tissue of the muscular coat.

There is no *muscularis mucosæ* in the mucous membrane of the pharynx; its place is taken by a layer of connective tissue which is exceedingly rich in longitudinal elastic fibres. This layer lies immediately upon the muscular coat, into which processes of fibro-elastic tissue extend between the muscular bundles; hence this fibro-elastic layer also serves as a submucosa.

The superficial layer of the corium contains diffuse collections of lymphoid tissue and occasional small lymphatic nodules.

The muscular coat of the pharynx is formed by its constrictor muscles. Their striated fibres mostly pursue an oblique course. Where these muscles are not immediately attached to the periosteum of the vertebræ, the pharynx is invested with an outer coat of areolar connective tissue by which it is loosely united to adjacent organs.

ESOPHAGUS

The wall of the esophagus contains the usual four coats: 1, the outer fibrous; 2, muscular; 3, submucous; and 4, mucous.

THE OUTER FIBROUS COAT envelops the wall of the esophagus and unites it to the adjacent organs. It consists of loose fibrous tissue, and contains the blood and lymphatic vessels and nerve trunks which supply the three inner coats.

THE MUSCULAR COAT contains an outer longitudinal and an inner circular layer of muscle fibres, which are separated by a narrow septum of loose fibrous tissue. In the upper and middle thirds of the esophagus the muscle is of the striated variety, in

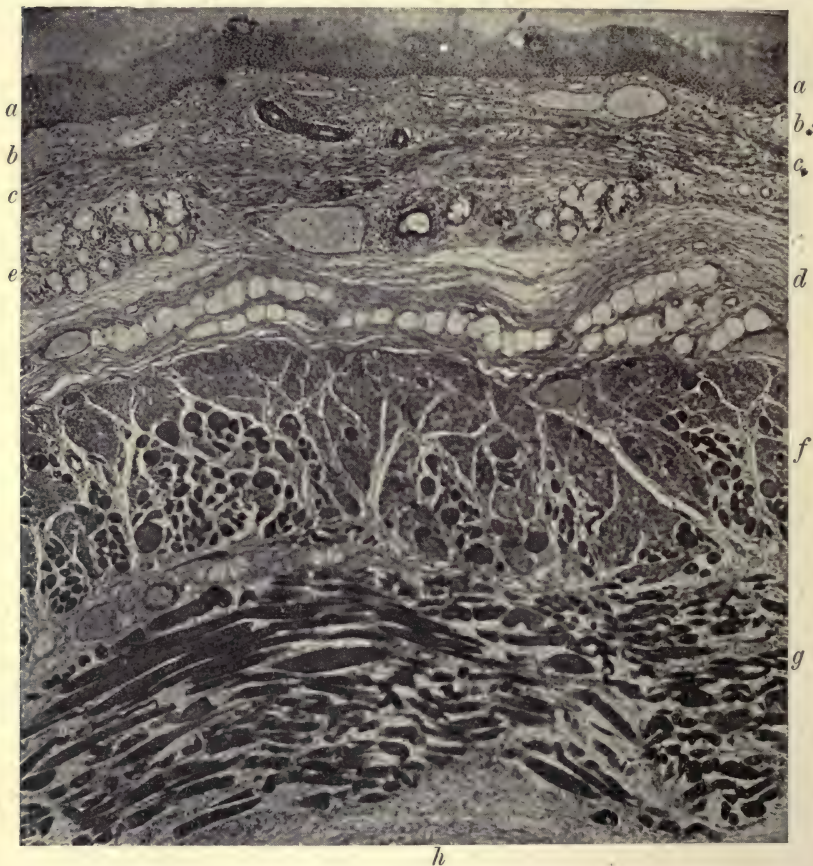


FIG. 227.—FROM A LONGITUDINAL SECTION AT THE JUNCTION OF THE MIDDLE AND LOWER THIRD OF THE HUMAN ESOPHAGUS.

a, epithelium; *b*, corium, and *c*, muscular layer of the mucosa; *d*, fibrous tissue, and *e*, mucous glands of the submucosa; *f*, inner, and *g*, outer layer of the muscular coat, the former partly of smooth and partly of striated fibres; *h*, edge of the outer fibrous coat. Hematein and eosin. Photo. $\times 42$.

the lower third it is largely smooth or involuntary muscle. The distribution of the muscle in the lower third is, however, subject to great individual variation, and occasional striated fibres are often found all the way down to the diaphragmatic opening.

The fibrous septum between the muscular layers contains the larger blood vessels and the nerve plexus of Auerbach.

THE SUBMUCOUS COAT forms a layer of areolar connective tissue which firmly unites the muscular and the mucous coats. It contains those blood and lymphatic vessels, together with the nerve plexus of Meissner, whose branches supply the mucous membrane. It also contains a considerable number of tubulo-acinar mucous glands whose ducts enter the mucous membrane and open upon the free epithelial surface. The secreting acini of these glands are short branching tubules with ampullary dilatations; they possess a characteristic, tortuous form. Their columnar secreting cells have a strong affinity for muchematein and other mucous stains. This basophile reaction, together with the situation of their isolated groups of secreting acini within the submucosa, sharply distinguishes the esophageal mucous glands from the secreting glands of the stomach and intestine.

THE MUCOUS COAT (*mucosa*) of the esophagus consists of a tunica propria or corium of areolar tissue which rests upon a well-developed muscularis mucosæ and is covered on its free surface by stratified squamous epithelium.

The muscularis mucosæ contains considerable bundles of smooth muscle whose general direction is a longitudinal one in its outer, and circular in its inner portion. This layer forms the outermost layer of the mucous coat, and is penetrated by the ducts of the deep mucous glands whose secreting acini lie in the submucosa.

The inner portion of the tunica propria carries on its surface many tall connective tissue papillæ which project well into the epithelial coat and which closely resemble the vascular papillæ of the skin.

The mid-portion of the corium is penetrated by the ducts of the mucous glands. These are at first lined by low columnar cells which, as they approach the epithelial surface are changed into several layers of flattened cells, which thus form a thin stratified lining, continuous with the superficial stratified squamous epithelium of the esophageal mucosa. Many of these ducts possess small cystic dilatations which are found in the connective tissue of the corium or occasionally in the submucosa.

Superficial Glands.—At about the level of the cricoid cartilage the esophageal mucous membrane presents two lozenge-shaped depressions, one on either side, whose diameter varies from 1 cm. down to a microscopical size. These areas mark the site of the

superficial glands of the esophagus (Hewlett*) or upper cardiac glands (Schaffer†). These are short branched tubular glands which closely resemble those of the cardiac region of the stomach.

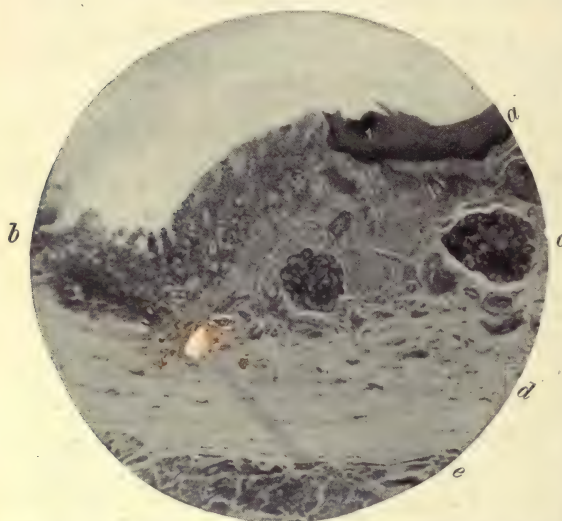


FIG. 228.—FROM A SECTION OF THE SUPERFICIAL GLANDS OF THE HUMAN ESOPHAGUS.

a, esophageal epithelium; *b*, superficial glands; *c*, mucous glands; *d*, tunica propria; *e*, muscularis mucosæ. Hematoxylin and eosin. Photo. $\times 17$. (After Hewlett.)

They are confined to the mucous membrane; their tubules, in marked contrast to those of the deep mucous glands of the esophagus, never penetrating the muscularis mucosæ, which, however, is considerably thinned beneath the superficial glands. These glands secrete a mucinous fluid, but their cells are not so strongly basophile as those of true mucous glands such as the deep glands of the esophagus.

The ducts of the superficial glands, as well as their secreting portions, and also the lining epithelium of the esophagus upon which they open, are clothed with columnar epithelial cells. Many of the secreting tubules contain parietal cells similar to those of the fundus glands of the stomach. Both ducts and secreting tubules contain small, cystic dilatations.

At the lower end of the esophagus a similar group of superficial glands, the *cardiac glands* of the esophagus, frequently mark the beginning transition to the structure of the cardiac portion of the stomach, with whose secreting glands they are continuous.

The lining epithelium of the esophagus is of the stratified squamous variety. Its attached surface is indented by the papillæ of the corium; its free surface is smooth. In the collapsed state of the organ its mucous membrane is thrown into longitudinal folds or rugæ and its lumen is obliterated. The small isolated areas of

* Jour. Exper. Med., 1901.

† Sitz. d. Wien. Akad., 1897.

columnar or ciliated epithelium, which occur in occasional individuals on the surface of the esophageal mucosa, especially in its upper third, are to be regarded as examples of irregular development.

THE STOMACH

THE SEROUS COAT of the stomach is derived from the peritoneum. It is formed by a thin layer of subserous connective tissue which is covered by endothelium. The serous coat supports

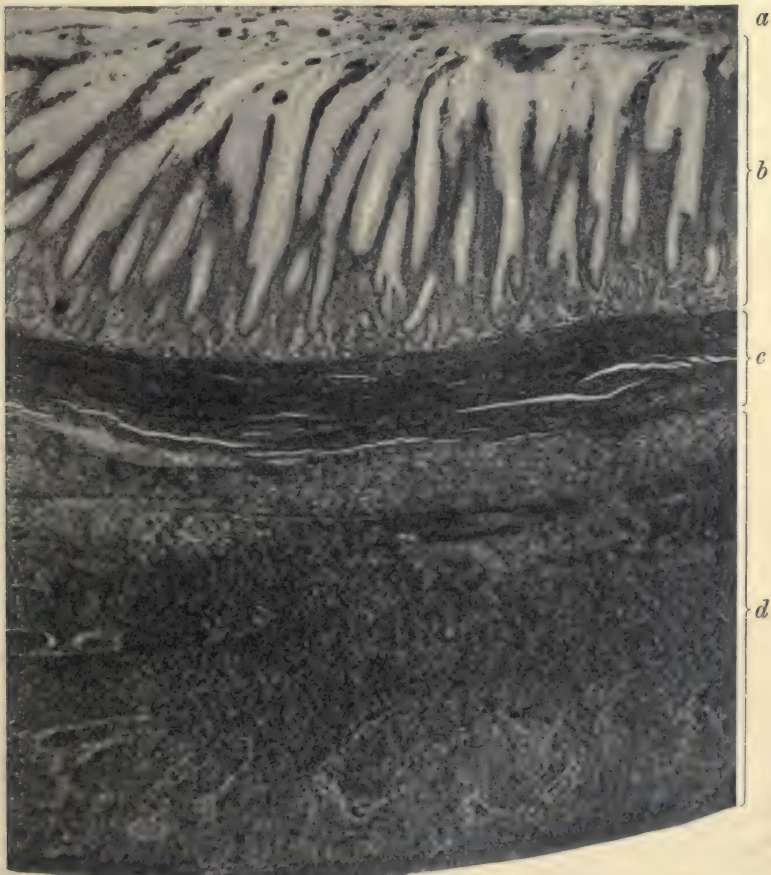


FIG. 229.—FROM A TRANSECTION OF THE WALL OF THE HUMAN STOMACH NEAR THE PYLORIC ORIFICE.

a, secretion; *b*, mucosa; *c*, submucosa; *d*, the very much thickened muscular coat. The serous coat was not included in the figure. Hematein and eosin. Photo. $\times 40$.

the larger blood and lymphatic vessels and nerve trunks which supply the organ.

THE MUSCULAR COAT of the stomach consists in general of two layers of smooth muscle fibres—a thin outer longitudinal, and a much thicker inner circular and oblique layer. The regular circular arrangement of these fibres is much distorted by the peculiar dilatation and partial rotation to which the stomach is subjected in the course of its development, and as a result of this change obliquely placed fibres form a considerable portion of the muscular coat.

The oblique fibres are most numerous toward the cardiac end of the stomach, where they form a third muscular layer, the innermost portion of the muscular coat. The longitudinal fibres are most abundant toward the cardiac and pyloric orifices and along the lesser curvature; in the fundus and mid-region of the stomach they form only a very thin layer. The circular fibres form the thickest of the three muscular layers and are nearly equally distributed in all portions, except that at the cardiac and pyloric orifices they become much thickened to form the sphincter muscles. The pyloric sphincter is especially well developed (Fig. 229).

The layers of the muscular coat of the stomach are united by thin septa of connective tissue; that between the longitudinal and circular layers contains the nerve plexus of Auerbach and the larger blood vessels which supply this coat.

THE SUBMUCOSA consists of loose areolar tissue which supports the blood vessels, lymphatics, and the nerve plexus of Meissner, all of which distribute their branches to the mucous membrane. In no portion of the stomach does this coat contain secreting glands.

THE MUCOUS COAT.—The muscularis mucosæ forms a thin but complete layer from one end of the stomach to the other, and marks the outer boundary of the mucous membrane. It usually consists of two thin layers, an inner circular and an outer longitudinal. Here and there muscle fibres extend from the muscularis mucosæ into the corium between the gastric glands.

The surface of the mucosa is clothed with tall columnar epithelium, and the whole membrane is thrown into wavy folds, an arrangement which is permitted by the very loose meshes of the submucous areolar coat. The corium of the mucosa is closely packed with tubular secreting glands, which open on the surface by wide-mouthed, crypt-like ducts or foveolæ, and are embedded in a fine fibro-reticular tissue containing many lymphatic corpuscles.

The character of the secreting glands differs somewhat in various portions of the stomach. The three varieties, according to their distribution, are known as the fundus glands, the pyloric glands, and the cardiac glands.

The Fundus Glands (*Peptic Glands*).—These are somewhat branched tubular glands which possess short ducts, the *crypts* or *foveolæ*, and relatively long secreting portions several of which open, by means of short constricted portions, the *necks* of the glands, into the bottom of each crypt.

The ducts or crypts are lined by tall columnar cells which possess a remarkably clear distal cytoplasm, and whose nuclei lie at the proximal or attached ends of the cells. This epithelium rests upon a distinct basement membrane of reticular tissue (Mall); it is also continued over that portion of the corium which occupies the intervals between adjacent ducts, where it forms the true *lining epithelium* of the stomach. Its cells secrete a clear muco-albuminous fluid.

The secreting portion, *fundus*, of the gland is five to eight times as long as the duct or foveola, a fact which sharply differentiates the fundus from the pyloric glands of the stomach. The lumen of the secreting portion is so narrow as to be scarcely perceptible except by the use of special stains or high magnification.

The fundus of the gland is lined by two distinct cell types, the chief and the parietal cells. The chief cells are relatively more

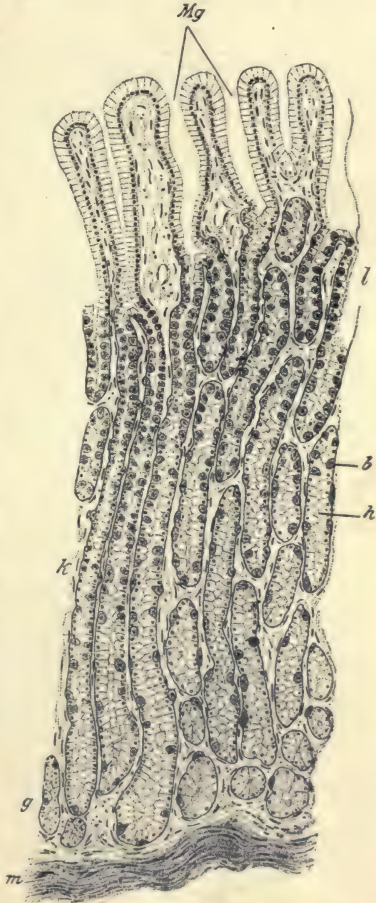


FIG. 230.—LONGITUDINAL SECTION OF THE FUNDUS GLANDS OF MAN.

b, parietal cells; *g*, fundus of the gland; *h*, chief cells; *k*, body, and *l*, neck of the gland; *m*, muscularis mucosæ; *Mg*, gastric crypts. $\times 85$. (After Kölliker.)

abundant at the deeper portion of the fundus, where they form a complete lining for the tubule. In this portion the parietal cells are crowded away from the lumen and consequently produce a bulging of the basement membrane. Toward the neck of the tubule



FIG. 231.—THE MUCOSA OF THE FUNDUS REGION OF THE DOG'S STOMACH.

a, gastric crypts; *b*, neck region, and *c*, fundus portions of the secreting glands, the parietal cells being much more abundant in the former; *d*, muscularis mucosae; *e*, submucosa. Hematein and eosin. Photo. $\times 80$.

the parietal cells are more abundant and draw progressively nearer and nearer *a* the lumen until, in the neck of the gland, they possess a considerable free surface which encroaches upon the glandular lumen. *b*

The Chief Cells (*central, peptic, or adelomorphous cells*) possess a cuboidal or pyramidal shape and a granular cytoplasm. The spheroidal nucleus is situated in the proximal or attached end, while the distal end of the cell is its most granular portion. *c* The breadth of the granular zone is dependent upon the state of secretory activity, the coarse zymogen granules accumulating during periods

of rest and disappearing by secretion during activity. Thus the granular distal zone increases in breadth during rest and decreases during activity. The whole cell, also, becomes shrunken after prolonged secretion, but during rest it becomes so swollen that with its neighbors it nearly occludes the lumen of the tubule.

The coarse *zymogen granules* within the cell appear to be suspended within the meshes of a finely granular cytoplasmic reticulum. At the base or proximal end of the cell coarse elongated granules of *prozymogen* (ergastoplasm of Cade) may be demonstrated by the stronger basic or nuclear dyes, e.g., iron hematein, toluidin blue. These peculiar prozymogen granules are so disposed, parallel to the axis of the cell, as to give this portion of the cytoplasm a somewhat striated or rodded appearance when carefully examined after suitable staining.

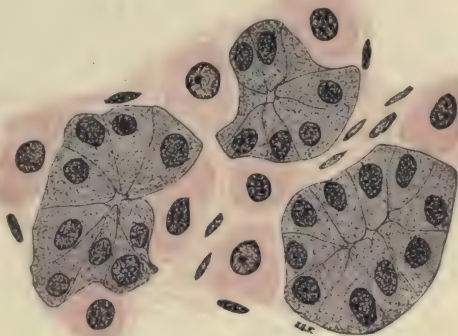


FIG. 232.—TRANSECTIONS OF THREE SECRETING GLANDS OF THE FUNDUS REGION OF THE HUMAN STOMACH.

The section is taken from the portion of the glands near the muscularis mucosæ. The parietal cells are red; the central cells, black. Hematein and eosin. $\times 800$.

The *Parietal Cells* (*oxyntic* or *delomorphous cells*) are large ovoid or pyramidal bodies which are frequently binucleated, and whose cytoplasm possesses a strong affinity for acid dyes (eosin, Congo red, etc.). Their spherical nuclei contain much chromatin and are centrally situated; their cytoplasm is homogeneous or finely granular.

The shape of the oxyntic cells varies with their location. At the fundus of the gland where they are separated from the lumen by the chief cells they are ovoid or occasionally triangular in transection, the broad base of their triangular section being applied to the basement membrane, the wide-angled tip wedged between the bases of the adjacent chief cells. In the mid-portion of the secreting tubule the parietal cells approach nearer the lumen, and, being inserted between the chief cells, they acquire an increased height and a pyramidal form. At the neck of the gland, where they present to the glandular lumen a broad surface, the parietal cells acquire a cuboidal shape. As the gland opens into its foveola the parietal cells, except for an occasional dislodged or misplaced individual, abruptly cease.

In those portions of the tubule where the parietal cells are

more or less removed from the lumen they possess an extensive system of pericellular *secretory canals* which invest the cell in a basket-like manner and convey its secretion to the glandular lumen, where it mixes with the secretion of the chief cells. The parietal cells also possess a system of intracellular canaliculi.

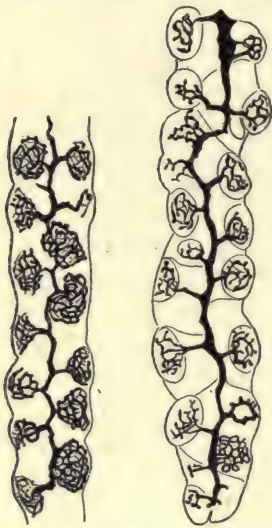


FIG. 233.—SECRETORY CAPILLARIES OF THE FUNDUS GLANDS OF THE DOG'S STOMACH.

Golgi stain. (After Müller, from Oppel.)

Pyloric Glands.—These are branched convoluted tubular glands with relatively long crypt-like ducts, into the bottom of which several secreting tubules open.

The typical convolution is found only in the fundus of the gland, the course of the ducts being nearly straight. The branching, on the other hand, is chiefly confined to the ducts, which occupy the superficial two-thirds to three-fourths of the entire depth of the mucous membrane. In the pyloric mucosa, therefore, *three zones* may be distinguished—a superficial, middle, and deep.

The superficial zone is narrow and contains the wide-mouthed crypts or foveolæ which are lined by tall columnar cells similar to those of the fundus crypts.

The middle zone contains the narrowed portion of the ducts and is the broadest of the three zones. Several of the narrow ducts open into each foveola and further branching of the secreting tubules occurs to a limited extent. The epithelium of the ducts is of the low columnar variety, whose deeply stained basal nuclei are spheroidal or ovoid, and are progressively flattened as the secreting portion is approached. The superficial cytoplasm of these cells stains readily with muchematein and often has a coarsely granular or reticular appearance.

The deepest zone contains the convoluted secreting portions and is sharply demarked from the adjacent ducts, since in a transection of the stomach wall its tubules, owing to their convolution, are nearly all cut across, while the ducts are in longitudinal section; the clear tall columnar epithelium and broad lumen of the fundus, also, contrast strongly with the low finely granular epithelium and narrow lumen of the duct. It is this narrow zone of

peculiar convoluted tubules, lying just within the muscularis mucosæ, by which the pyloric mucous membrane is most readily distinguished from all other regions of the alimentary tract.

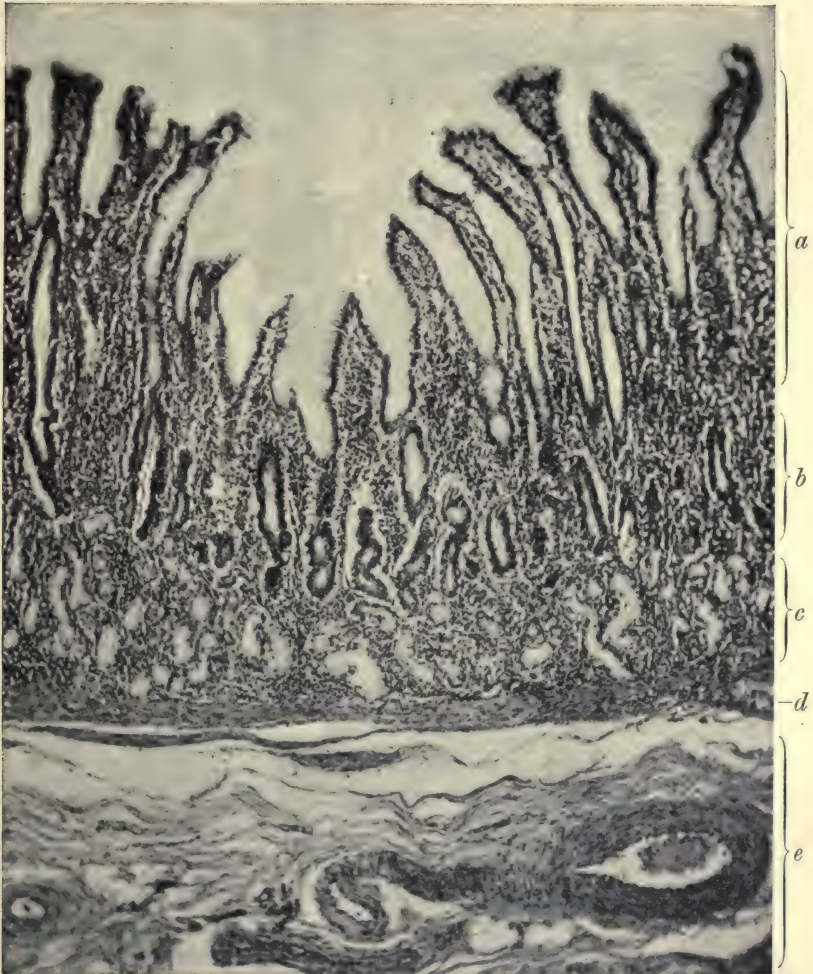


FIG. 234.—THE MUCOSA OF THE PYLORIC REGION OF THE HUMAN STOMACH.
a, *b*, and *c*, respectively the crypt, neck, and fundus zones of the secreting glands; *d*, muscularis mucosæ; *e*, submucosa. Hematein and eosin. Photo. $\times 151$.

The tall columnar cells of the fundus possess a remarkably clear cytoplasm which reacts distinctly, though feebly, to the spe-

cific stains for mucus. The nuclei are flattened against the base of the cell and thus contrast sharply with the spheroidal nuclei of the ducts and crypts.

During secretion the cells become shrunken and their nuclei approach the center of the cell and become more nearly ovoid or spheroidal in shape.

There is no sharp demarcation between the fundus and pyloric regions, the glands offering a gradual transition from the one type to the other. Thus, in the human stomach, there is a broad transition zone which contains both fundus and pyloric glands. Indeed, in many individuals, parietal cells may be distributed throughout almost the entire gastric mucosa.

The Cardiac Glands.—A narrow region at the cardiac orifice of the human stomach contains glands whose form corresponds with that of the fundus glands, though they are slightly more branched and are rather more tortuous, but which are lined by relatively clear columnar epithelium. Only occasionally are the chief and the parietal cells, which are characteristic of the fundus glands, interspersed among the clear secreting cells of these tubules. The cardiac glands, therefore, appear to offer a transition from the esophageal to the more numerous fundus glands of the stomach. In certain mammals, e. g., the pig and the marsupials, the cardiac glands occupy a much larger area.

The Corium of the mucosa consists of a delicate fibro-reticular connective tissue which supports the blood and lymphatic vessels and is more or less infiltrated with lymphatic corpuscles. Hence in many portions it possesses the character of diffuse lymphoid tissue, though this tissue is characteristic of the interglandular, rather than the interfoveolar, portion of the tunica propria. In the latter situation, in sharp contrast to the intestinal villi, with which the student readily confounds this region, the corium is decidedly fibrous and contains relatively few lymphatic corpuscles.

In the deeper part of the mucosa occasional small lymphoid nodules, homologues of the solitary follicles of the intestine, are seen. These nodules* lie just within the muscularis mucosæ and do not, as a rule, penetrate into the submucosa. In the cardiac region they may lie very near the free surface of the mucosa.

* The name, *lenticular glands*, formerly applied to these lymphatic nodules, is misleading and should be discarded.

BLOOD SUPPLY.—The large blood vessels, derived from the branches of the celiac axis, enter through the subserous connective tissue of the omentum and form arches at the greater and lesser curvatures of the stomach.



FIG. 235.

FUNDUS REGION OF A DOG'S STOMACH, BLOOD VESSELS INJECTED.
A, artery; *G*, inner layer, and *L*, outer layer of the muscular coat;
M, mucosa; *S*, submucosa; *V*, vein. Diagrammatic. (After Mall.)

From these arches, arteries lying in the subserous connective tissue are distributed to the ventral and dorsal surfaces of the gastric wall. These vessels supply branches which penetrate the muscular coat, giving off, on the way, arterioles to the intramuscular septum, and secondarily to the intramuscular capillary plexus, and spread out in the areolar tissue of the submucosa in which they form an extensive arterial plexus. Branches from this submucous plexus enter the mucous membrane and form a dense capillary plexus whose elongated meshes inclose the secreting glands.

Near the surface of the mucosa these vessels enter a plexus of small venules which, by union, form larger branches and convey the blood outward to a venous plexus at the outer border of the mucosa, whence it returns to the larger veins of the submucosa. These veins, after receiving venules from the muscular coat, pass outward to the subserous connective tissue in company with the entering arteries and finally reach the gastric, splenic, and portal veins.

THE LYMPHATICS arise by vascular loops or dilated extremities between the secreting glands of the mucosa. At the outer border of the mucous membrane they form a delicate anastomosing plexus from which branches penetrate the muscularis mucosæ and enter a broader submucous plexus whose efferent vessels pierce the muscular coat on their way to lymphatic glands which are situated in the folds of the omentum at either curvature of the stomach.

THE NERVES of the stomach are derived from the sympathetic and pneumogastrics. They enter with the blood vessels and pierce the muscular coat to form two plexuses of anastomosing nerve trunks; the one (Auerbach's) in the intramuscular fibrous septum contains ganglionic enlargements at many of its intersections and distributes its fibrils to the smooth muscle; the other (Meissner's), lying in the deeper part of the submucosa also contains small ganglia at the intersections of its anastomosing branches. This latter plexus is much finer than that of the muscular coat; it distributes its fibrils to the mucosa, where they terminate in and about the walls of the blood and lymphatic vessels and beneath the epithelium of the secreting glands.

SMALL INTESTINE

The structure of the *serous coat* of the small intestine is identical with that of the stomach. The *muscular coat* consists of an

inner and an outer layer of smooth or involuntary muscle fibres which are separated by a thin connective tissue septum. The inner circular layer is much thicker than the outer longitudinal.

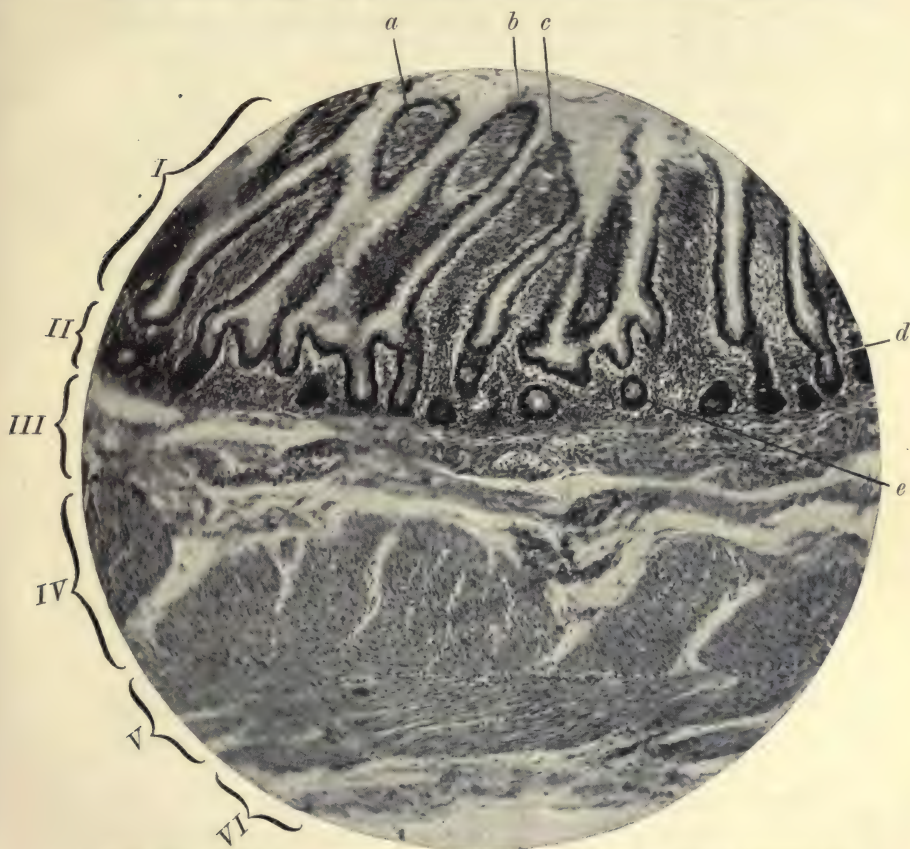


FIG. 236.—FROM A LONGITUDINAL SECTION THROUGH THE WALL OF THE HUMAN SMALL INTESTINE.

I, villi, and *II*, crypts of the mucosa; *III*, submucosa; *IV*, circular, and *V*, longitudinal layer of the muscular coat; *VI*, serous coat; *a*, *b*, and *c*, villi in transverse, oblique and longitudinal section, respectively; *d*, crypts in longitudinal, and *e*, in transverse section. Hematein and eosin. Photo. $\times 160$.

The regular disposition of the muscle fibres as an outer longitudinal and an inner circular layer serves as a guide to the recognition of the direction in which a given microscopical section has been cut. In transections of the intestine the muscle fibres of the outer layer of the muscular coat are transversely cut; in longitu-

dinal sections of the organ the same fibres are seen in longitudinal section.

The submucosa, of areolar connective tissue, is identical with that of the stomach except in the duodenum where it is penetrated by the branched tubulo-acinar glands of Brunner. The muscularis mucosæ forms a complete muscular layer and, except in the duodenum, is not penetrated by the secreting glands.

The Mucous Membrane of the small intestine is divisible into an inner and an outer zone. In the inner zone the corium forms finger-like projections, the intestinal *villi*, which are covered with tall columnar epithelium containing many mucus secreting, goblet cells. The villi are characteristic of the small intestine, in which alone they occur. They serve to increase the area of the lining epithelium of the intestine, whose chief function is that of absorption.

The outer zone of the mucous membrane includes all that portion between the muscularis mucosæ and the bases of the intestinal villi. It is almost completely occupied by the simple tubular glands or crypts of Lieberkühn.

The corium of the small intestine, in which the crypts of Lieberkühn are embedded, and which forms the substance of the intestinal villi, consists of a fibro-reticular stroma which is so infiltrated with leucocytes as to form a diffuse lymphoid tissue. In many parts of the mucosa the lymphoid tissue forms isolated nodules, the *solitary follicles*, or aggregations of such nodules, which are known as the *agminated follicles* or *Peyer's patches*. Solitary follicles occur throughout both the large and the small intestine. Peyer's patches are found only in the small intestine and are most numerous in the upper portion of the ileum.

The structure of the **solitary follicles** does not differ from that of other lymphoid nodules. They vary much in size, most of them being of sufficient diameter to occupy the entire thickness of the mucous membrane. They push aside the adjacent crypts of Lieberkühn by which they are encircled, and few or no villi project from their free surface. The adjacent villi are so inclined that their free ends often hide all but the projecting apex of the ovoid solitary follicle.

The largest of the solitary follicles not only produce a distinct elevation of the surface of the mucous membrane but may even break through the muscularis mucosæ and project into the connective tissue of the submucosa. The solitary follicles, like other lymphoid nodules, usually contain a germinal center.

Peyer's patches (*agminated follicles, agminated glands*) are formed by accumulations of lymphatic nodules, usually occurring in that portion of the intestinal mucosa which is farthest removed from the attachment of the mesentery. They frequently form oval areas of macroscopic size. The number of their constituent

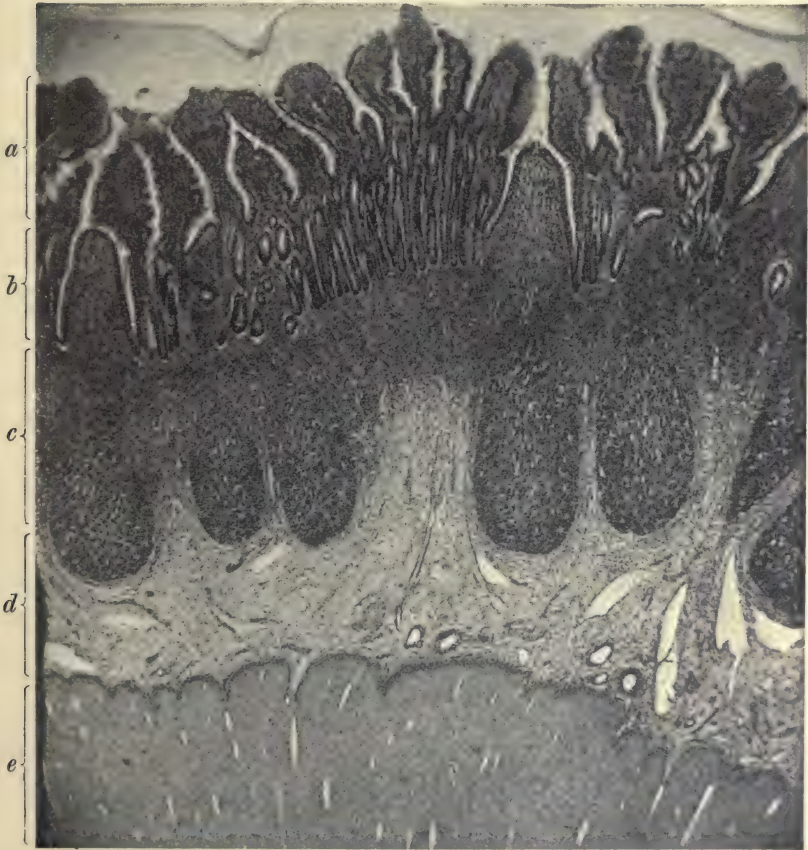


FIG. 237.—THE CENTRAL PORTION OF A PEYER'S PATCH IN THE ILEUM OF A DOG'S INTESTINE.

a, villi; b, crypts; c, lymphoid nodules, an agminated follicle; d, connective tissue of the submucosa; e, a portion of the muscular coat. Hematein and eosin. Photo. $\times 35$.

nodules is variable, frequently they contain as many as fifteen or twenty. Each of these nodules is usually invested by a thin fibrous capsule, though frequently they are confluent with one another.

The long axes of the ovoid nodules exceed the average thickness of the mucous membrane so that the patch forms a superficial elevation of the mucosa and its deeper surface penetrates the muscularis mucosæ and enters the submucous coat. Hence occasional fragments of the muscularis mucosæ often occur between the bases of the constituent nodules; villi are found upon the free surface of the follicles only in the intervals between the constituent nodules. The largest of the nodules lie near the center of the patch, the smallest are found at its periphery.

Above the level of the ileum the largest collections of lymphoid tissue in the intestinal mucosa occur in the upper part of the duodenum, where there are extensive infiltrations of dense lymphoid tissue many of which contain typical nodules with germinal centers. These masses of lymphoid tissue are penetrated by the ducts of Brunner's glands, whose secreting portions form a bed upon which the lymphoid tissue rests. The duodenal patches differ slightly from those in the ileum in that they form a more confluent mass with relatively fewer nodules, possess a more diffuse character, are more deeply situated, and are therefore covered by the corium of the mucosa which contains both crypts and villi.

THE INTESTINAL VILLI are long finger-like projections which vary much in form in different mammals and in different portions of the tract in the same individual. They are, perhaps, most highly developed in the dog, where they form long projections with expanded or clubbed extremities and a constricted base or neck.

In man the villi are of a more conical shape, the base being, as a rule, slightly broader than the free extremity. In the duodenum of man they possess a foliate shape, in the ileum they are conical or somewhat clavate.

The villus is formed by a projection of the corium which is covered by the lining epithelium of the intestine. The axis of the villus contains a large lymphatic capillary or *lacteal*, which begins in the inner third and proceeds outward through the corium to enter a lymphatic plexus lying just within the muscularis mucosæ. In the base or outer portion of the villus the lacteal is surrounded by small groups of smooth muscle fibres which are disposed in an axial direction, and which are ontogenetically derived from the muscularis mucosæ. Many of these fibres turn outward and are attached to the basement membrane beneath the epithelium at the sides and tip of the villus. By their rhythmic contraction

the muscle fibres of the villus aid in expelling the contents of the lacteal.

The body of the villus consists of diffuse lymphoid tissue having a reticular stroma in which the lacteal, the muscle fibres, and the blood vessels are embedded.

Each villus is supplied with one or more arterioles which enter at the base and pass to the inner third, where they form an abundant capillary plexus about the blind extremity of the lacteal and

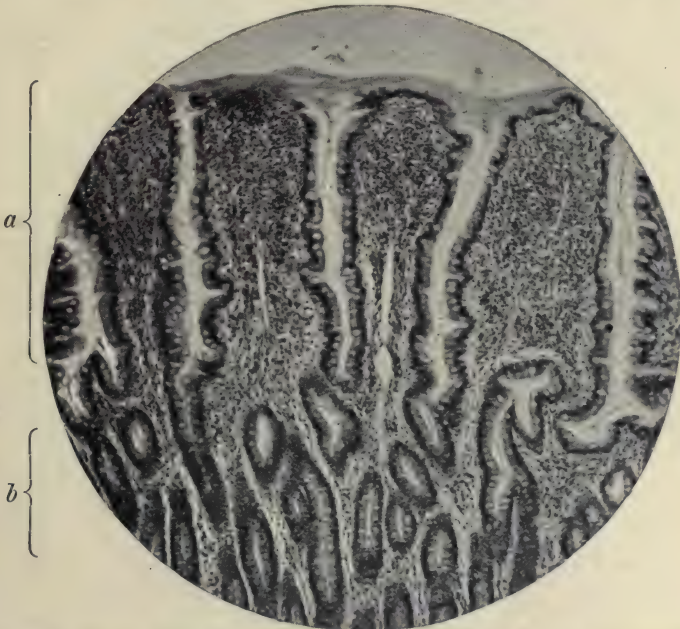


FIG. 238.—SEVERAL VILLI FROM THE SMALL INTESTINE OF THE DOG, IN LONGITUDINAL SECTION.

a, villi; *b*, crypts of Lieberkühn. Hematein and eosin. Photo. $\times 185$.

in the apex of the villus. Minute venules collect the blood from this plexus, and, following the course of the lacteal, make their exit from the base of the villus to join the venous plexus in the deeper part of the mucosa.

The lining epithelium of the intestine, which also clothes the villi, rests upon a distinct reticulated basement membrane and consists of columnar and goblet cells. The large number and peculiar appearance of the goblet cells is highly characteristic of this tissue.

The columnar cells are peculiar in that they possess a characteristic striated cuticular border when examined under moderately high magnification. They possess a finely reticular cytoplasm and an ovoid nucleus which is situated at the proximal end or base of the cell. Frequently the cytoplasm contains droplets of fat which are in process of absorption. Occasional leucocytes find their way into the epithelial coat, whence they may penetrate the intercellular substance and enter the intestinal canal.

The *intestinal glands* include two types, the tubulo-acinar glands of Brunner and the simple tubular glands of Lieberkühn. The former occur only in the duodenum; the latter are found in all portions of the intestine from the pylorus to the rectum.

THE GLANDS OF LIEBERKÜHN (*mucous crypts*) are simple tubules which extend the whole depth of the mucous membrane and open upon the free surface between the bases of the villi. Hence the lining epithelium of the glands becomes continuous with that which clothes the villi. The mucous crypts are embedded in the diffuse lymphoid tissue of the corium; they rarely branch. They consist of a lining epithelium and a basement membrane.

The epithelium of the crypts contains three types of cells: 1, *columnar cells*; 2, *goblet cells*; and 3, the *granule cells* of Paneth. The columnar and goblet cells resemble those which clothe the villi. The columnar cells which line the neck of the crypts possess a very indistinct cuticular border which is not found in the fundus cells of the glands. The epithelium of the crypts appears to take no part in the process of absorption and therefore contains no fat globules.

At the neck of the gland the epithelium frequently contains mitotic figures which have been demonstrated in man (Schaffer*) as well as in the lower mammals (Bizzozero†). Little or no mitosis has been demonstrated in the fundus of the gland or upon the free surface of the villi. On these facts the so-called "*wander theory*" of Bizzozero is founded. According to this theory there exist in the neck of the crypts certain indifferent cells which are capable of reproduction by mitosis and whose daughter cells move toward the free surface, being at the same time differentiated into either the goblet or the columnar cells of the villi.

Bizzozero originally considered that the granule cells of Paneth at the fundus of the crypts were intermediate phases in the formation of goblet cells, but as there is little or no mitosis in the

* Sitz. d. k. Akad. Wissensch., Wien, 1897.

† Arch. f. path. Anat., 1887.

region where these peculiar cells occur and as the granule cells are never displaced toward the surface, it seems more probable that, as also in the gastric glands, the indifferent genetic cells of the neck of the tubule develop on the one hand the superficial goblet and columnar cells which clothe the villi, and, on the other hand, the true secreting cells in the fundus of the glands of Lieberkühn.

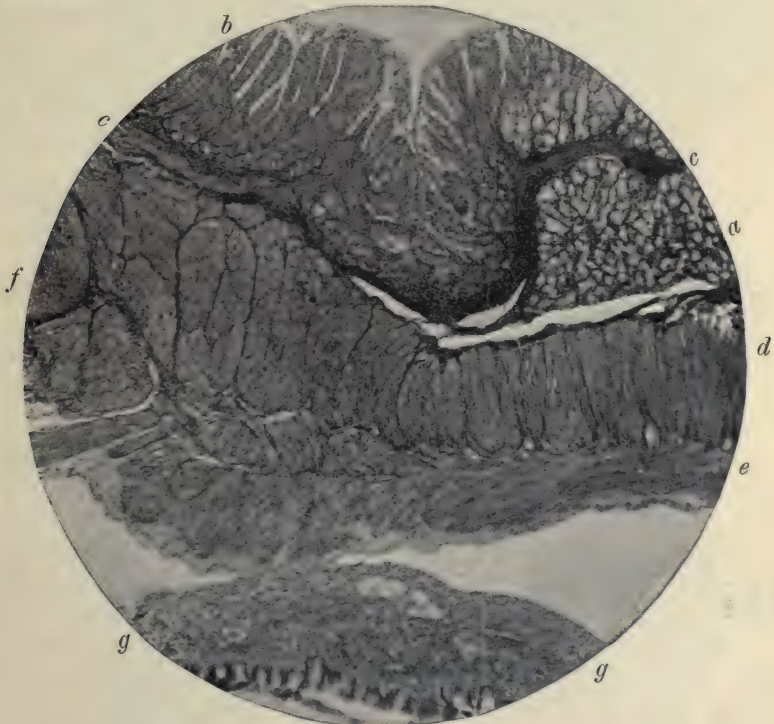


FIG. 239.—FROM A LONGITUDINAL SECTION OF THE "PYLORIC VALVE" OF MAN.

a, glands of Brunner; *b*, pyloric mucosa; *c-c*, muscularis mucosæ; *d*, inner layer of the muscular coat; *e*, outer layer of the muscular coat; *f*, muscular thickening at the pylorus; *g*, common bile duct. Hematein and eosin. Photo. $\times 48$.

The granule cells of Paneth* are confined to the extreme tip or blind extremity of the fundus of the mucous crypts. They are pyramidal or low columnar cells whose spheroidal nuclei are situated close to the basement membrane. Their cytoplasm presents a delicate reticulum which is filled with coarse granules which in

* Arch. f. mik. Anat., 1888.

some cells are of a basophile nature (Klein*). In others they contain still coarser granules which are strongly eosinophile. The exact function of these peculiar cells is unknown, but that they are true secreting cells seems highly probable.

The crypts of Lieberkühn are confined to the narrow deeper zone of the intestinal mucous membrane. Their lumen, after fixation, contains only the coarsely reticular mucous secretion.

The student should be warned to distinguish carefully between the transverse sections of the tubular crypts which are confined to the *deep* zone of the mucous membrane and the similar sections

of the villi which are only found in the *superficial* zone and whose epithelial coat, instead of inclosing a mere reticular mass of mucous secretion invests an organized body of diffuse lymphoid tissue.

THE GLANDS OF BRUNNER

are tubulo-acinar glands which furnish a muco-albuminous secretion. They appear to represent the continuation into the intestine of the pyloric glands of the stomach, and they occur in decreasing proportion throughout the entire length of the duodenum. They are, however, sharply distinguished from the pyloric glands by their large size, the secreting portions of Brunner's glands being only found in the submucosa and the deeper part of the mucous membrane, where their secreting acini form innumerable groups, the tubules of each of which are connected with the terminal subdivision of a duct.

The ducts of Brunner's glands open on the free surface between the villi by means of crypt-like tubules



FIG. 240.—RECONSTRUCTION MODEL OF A BRUNNER'S GLAND, FROM THE HUMAN DUODENUM.

Three partially blended ducts pass into the submucosa and end in expanded alveoli. $\times 344$. (After Maziariski.)

which are lined by tall columnar epithelium and can only with difficulty be distinguished from the adjacent crypts of Lieberkühn. In the deeper part of the mucous membrane the ducts

* Am. Jour. Anat., 1902, Proc. Am. Assoc. Anat.



FIG. 241.—BRUNNER'S GLANDS IN THE DUODENUM OF MAN.

a-a, villi and crypts, the former somewhat niacerated by post-mortem digestion; *b-b*, muscularis mucosæ; *c*, fat in the deeper part of the submucosa; *d*, margin of the muscular coat. Hematein and eosin. Photo. $\times 45$.

branch and pursue a somewhat tortuous course to the fundus of the gland, where the terminal acini of each subdivision of the duct are invested with a distinct fibrous capsule.

The secreting epithelium of Brunner's glands consists of tall columnar cells which surround a wide lumen. When loaded with secretion the cells are swollen and clear, but become shrunken and granular after a period of activity. Their cytoplasm reacts to the specific stains for mucin only when these are applied for a considerable time in concentrated solutions (Bensley). The spheroidal nucleus is situated at its proximal or basal end and as the cell fills with secretion the nucleus becomes progressively flattened.

BLOOD SUPPLY.—The blood supply of the small intestine resembles that of the stomach. The branches of the mesenteric arteries pass around the intestinal wall in the subserous connective tissue. From this point they penetrate the muscular coat to form intramuscular and submucous plexuses. From the latter a few branches supply the adjacent portion of the inner layer of the muscular coat, but most of them pass to the mucous membrane, in which a plexus lies just within the muscularis mucosæ and

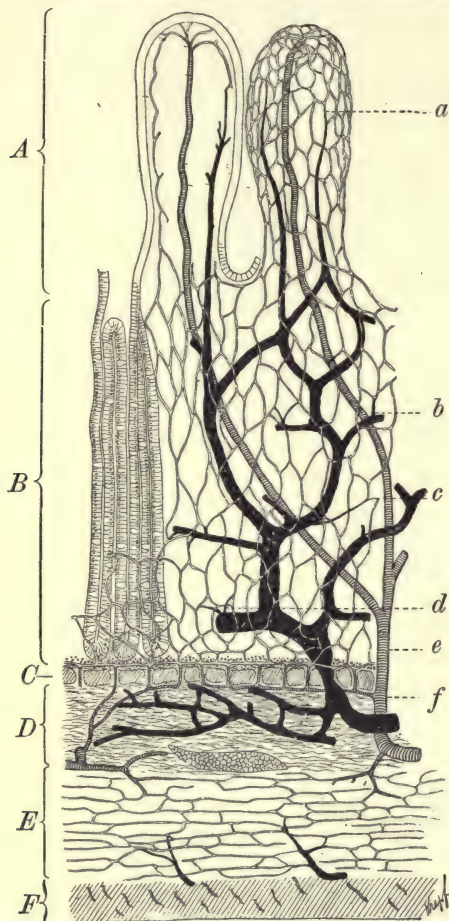


FIG. 242.—THE BLOOD VESSELS OF THE SMALL INTESTINE OF A DOG, DRAWN AFTER AN INJECTED PREPARATION.

The arteries are striped, the veins black, the capillaries open. A, villi; B, crypts; C, muscularis mucosæ; D, submucosa; E, circular, and F, longitudinal layer of the muscular coat; a, venule beginning from the capillaries of the villus, and at b, from those among the crypts; c, artery to the villus; d, venules in the deeper part of the mucosa; e, main arterial trunk to several adjacent villi; f, arterial branch to the glandular region. Highly magnified. (After Mall, from Oppel.)

distributes its branches to the capillaries about the crypts of Lieberkühn and to the intestinal villi.

The artery of the villus enters at its base, and, distributing capillaries along its course, forms in the distal part of the villus an abundant capillary network from which efferent venules return by a similar course. The artery, however, is found near the axis, the venules near the periphery of the villus.

Branches from the submucous and mucous arterial plexuses also supply capillaries to the glands of Brunner in the duodenum as well as to the solitary and agminated lymphatic follicles. About each of the lymphatic nodules they form circular anastomoses from which radial capillaries are distributed within the follicle.

The veins pursue a course exactly similar to that of the arteries. On their way to the mesenteric vessels they form mucous, submucous, intramuscular, and subserous plexuses.

LYMPHATICS.—The lymphatics or *lacteals* of the small intestine begin in the distal part of the villi as lymphatic capillaries, each having, as a rule, a pouched, blind extremity. At their origin the lacteals are frequently branched, or they may even form a scanty anastomosis. They finally unite to form a central lacteal in the axis of the villus, which empties into a rich plexus about the crypts of Lieberkühn, or, like the efferent vessels of this plexus, they may pass directly to the larger lymphatic vessels of the submucosa.

From the submucous plexus numerous efferent lymphatic vessels penetrate the muscular coat, receiving the lymph from the vessels of the intramuscular septum. They empty into the larger lacteal vessels of the mesentery which are intimately connected with numerous mesenteric lymphatic glands. In the mucosa and submucosa the lacteals form sinuses which surround the bases of the nodules of the solitary and agminated follicles. Thus, much of the chyle is permitted to come into relation with the parenchyma of these organs before leaving the intestinal mucosa.

NERVE SUPPLY.—The nerve supply of the intestine is exactly similar to that of the stomach. The non-medullated fibres form an intramuscular ganglionic plexus (Auerbach's) for the supply of the muscular coat, and a submucous plexus (Meissner's) which supplies branches to the blood vessels and to the glands of the mucosa. The finer branches in the mucous membrane penetrate to the villi, forming a delicate plexus of naked fibrils about its blood vessels and lacteals, and beneath its epithelium.

INTESTINAL ABSORPTION.—The absorption of fat consists essentially of *three phases*: 1, its absorption into the intestinal epithelium; 2, its secretion into the lymphoid tissue of the villus; and 3, its entrance into the lacteal vessels. In an animal killed

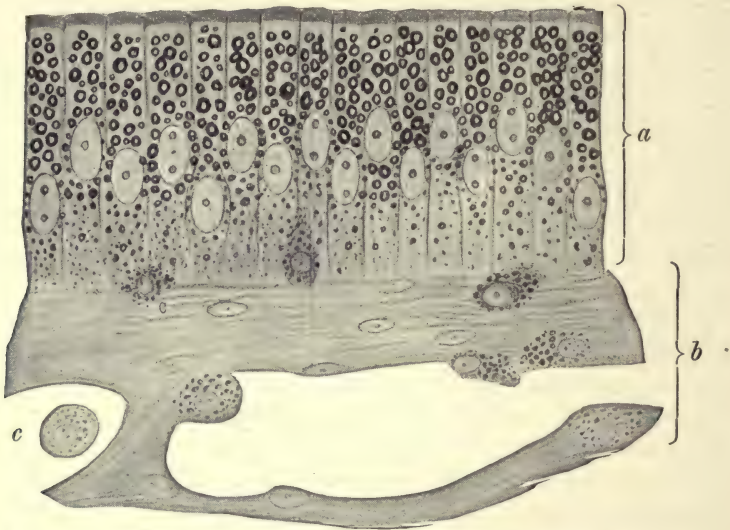


FIG. 243.—INTESTINAL MUCOSA OF A FROG DURING THE ABSORPTION OF FAT.

a, epithelium; *b*, tunica propria; *c*, an amœboid leucocyte. Osmium tetroxid. Highly magnified. (After Schäfer.)

during the absorption of fat, the intestinal villi, after fixation by solutions of osmium tetroxid, contain fat in (*a*) the epithelium, (*b*) the lymphoid tissue, and (*c*) the central lacteal.

In the epithelium fat is contained in the form of fine droplets which are most numerous in the distal or free ends of the cells. They are also found in the intercellular spaces. During absorption the epithelial cells of the villi become much swollen and elongated. As the process subsides they return to their former size, relatively they are shrunken. When most distended the intracellular fat droplets are the most abundant; as the cells shrink the intercellular droplets relatively increase in number (Drago*). The relative size of the epithelial cells and the abundance of intra-epithelial fat is apparently dependent upon the activity of the processes of absorption.

* Recherche d. lab. anat. norm. d. r. univ. d. Roma, 1900.

As to the manner in which the fat enters the epithelium there is some doubt. Schäfer* suggested that the leucocytes by their amœboid activity inclose the emulsified droplets in the intestinal lumen and convey them into the substance of the villi. It seems more probable that the fats are saponified in the intestinal tract, and, as such, enter the epithelium in solution. Here they are again synthesized into neutral fat by the activity of the epithelium (Pflüger†). Such a process accounts for the abundance of fat within the distal portions of the cells. The droplets are then secreted into the intercellular and subjacent tissue spaces.

The second phase of absorption includes the transference of the fat particles to the lacteal. This process appears to depend partially, at least, upon the activity of the leucocytes, as suggested by Schäfer, the particles of fat thus finding their way through the diffuse lymphoid tissue. According to Reuter‡ fat droplets are found in the tissue spaces as well as in the lymphatic corpuscles of the diffuse lymphoid tissue, a fact which would seem to indicate that other agencies aid in the transit of the fat from the epithelium to the lacteal than are accounted for by the purely mechanical theory of Schäfer.

The third phase includes the secretion of the fat into the lumen of the lacteal. This is, at least partially, accomplished by the disintegration of fat-laden leucocytes which, by amœboid motion, have found their way into the lacteal. Other fat particles may possibly find their way into the lacteal without the aid of the leucocytes, a process which may be

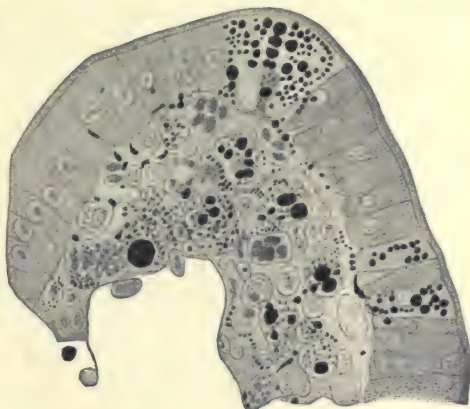


FIG. 244.—APEX OF AN INTESTINAL VILLUS OF A RABBIT WHICH HAD BEEN FED WITH MILK.

The fat droplets have been blackened by fixation with picric acid and osmium tetroxid. The figure shows the distribution of fat during certain stages of absorption. Alum carmin stain. Highly magnified. (After R. Heidenhain, from Oppel.)

* Internat. Monatsch. f. Anat. u. Physiol., 1885.

† Arch. f. d. ges. Physiol., 1900.

‡ Anat. Hefte, 1902.

more or less dependent upon the vital properties of the lining epithelium.

The absorption of the products resulting from the digestion of the starches, sugars, albumins, etc., probably proceeds along similar lines. The peptones enter the epithelium in solution and are then secreted, as albumins and globulins, into the tissue spaces, whence they find their way into the lacteal and capillaries. Thus the lacteals become widely distended even in the absence of the digestion and absorption of fat.

THE LARGE INTESTINE

The three outer coats of this portion of the alimentary canal are identical in structure with those of the small intestine, with a

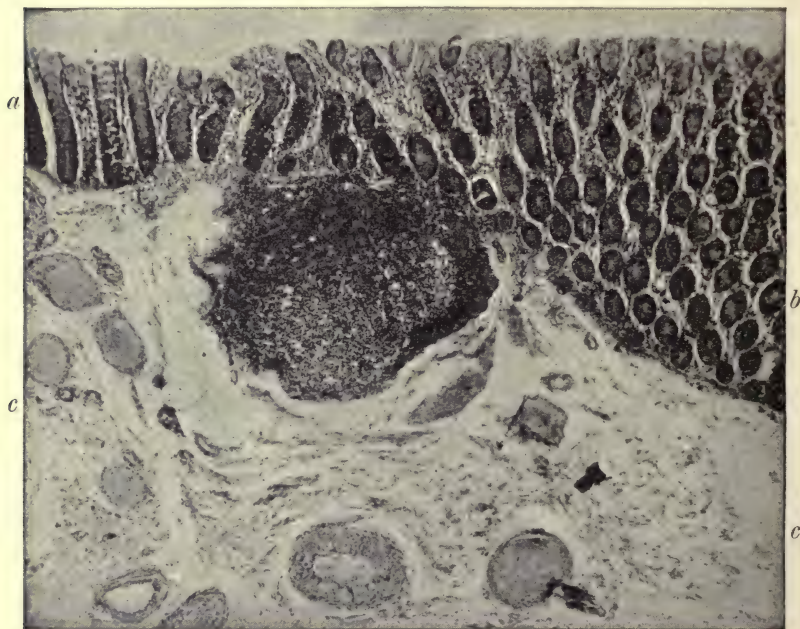


FIG. 245.—THE MUCOSA OF THE LARGE INTESTINE OF MAN.

At *a*, the crypts are in longitudinal section; at *b*, owing to a fold of the mucosa, they are very obliquely cut, some of them being almost in transection. A single solitary nodule of lymphoid tissue is embedded in the superficial portion of the submucosa; *c, c*, the vascular submucosa. Hematein and eosin. Photo. $\times 48$.

single exception in the irregular distribution of the outer layer of the muscular coat, which in the large intestine forms three distinct longitudinal ridges or thickenings. At other parts of the

circumference of the organ the outer muscular layer is slightly thinner than in the small intestine.

The mucous membrane of the large intestine may be best described by comparison with that of the small intestine. If the mucosa of the latter organ contains two zones, a superficial layer of villi and a deeper glandular layer, that of the large intestine may be said to consist of only the deeper of these zones. It therefore possesses no villi, and its simple tubular crypts of Lieberkühn extend from the free surface almost to the muscularis mucosæ.

The lining epithelium of the large intestine is of the simple columnar variety and has only an indistinct cuticular margin. That of the crypts of Lieberkühn contains both columnar and goblet cells, the latter being far more numerous than in the small intestine.

The lymphoid tissue of the large intestine occurs in the form of diffuse lymphoid tissue in the corium, and as solitary follicles, which frequently break through the muscularis mucosæ and lie in the submucosa. The fundus of such crypts of Lieberkühn as may occasionally be inclosed within the lymphatic follicles are frequently prolonged into the superficial portion of the submucosa where they often possess alveolar dilatations. Elsewhere the muscularis mucosæ forms a complete membrane which is nowhere penetrated by the simple tubular glands of Lieberkühn.

Lymphatic nodules are especially abundant in the rectum and in the **vermiform appendix**. In the latter the nodules are more or less confluent, a condition which is not found elsewhere in the large intestine. In the appendix the greater portion of the mucous membrane is invaded by the lymphoid tissue and the crypts are much diminished in both number and size (Fig. 246).

The vascular and nerve supply of the large intestine is identical in its arrangement with that of the small intestine. The mucous membrane contains a capillary plexus of blood and lymphatic vessels in the corium about the crypts. The nerves of the large intestine supply its muscular coats and blood vessels and, in the mucosa, end in naked varicose or knobbed fibrils beneath the epithelium of the glands of Lieberkühn.

In the rectum the lining epithelium is continuous at the anus with the stratified squamous epithelium of the skin. In this region, also, the circular fibres of the inner layer of the muscular coat are much thickened to form the internal rectal sphincter. Lymphoid tissue abounds in the rectal mucous membrane.

The ileo-cæcal valve, which guards the orifice by which the small intestine opens into the cæcum, is formed by a reduplication of the mucous membrane, which is strengthened by a thickening and overlapping of the circular muscular layers of both small and large intestines.

The outer longitudinal muscular layer is continued directly from the wall of the ileum to that of the cæcum, and therefore



FIG. 246.—TRANSECTION OF THE VERMIFORM APPENDIX OF MAN.

The submucosa contains much adipose tissue, and a number of large lymphoid nodules, each with a dense periphery and a large, lighter, germinal center. Photo. $\times 10$.

pursues a relatively shorter course than either the internal muscular layer or the mucous membrane. Section of only the outer layer of the muscular coat permits one to straighten the fold of the intestinal wall and thus obliterate the valve. In other words the outer muscular layer is not included in the valvular reduplication.

The muscularis mucosæ is slightly thickened at the margin of the valve. At this point, also, the villi become shorter and at the margin of the cæcal surface of the valve they entirely disappear.

The following tabulated statement of the more important characteristics of the several portions of the alimentary tract may be of assistance to the student in the differential diagnosis of these organs.

	ESOPHAGUS.	CARDIAC STOMACH.	FUNDUS STOMACH.	PYLORIC STOMACH.	DUODENUM.	ILEUM AND JEJUNUM.	LARGE INTESTINE.
Lining epithelium.....	Stratified squamous.	Columnar.	Columnar.	Columnar.	Columnar and goblet.	Columnar and goblet.	Columnar and many goblet.
Glandular epithelium...	Columnar, mucous.	Muco-albuminous, few parietal cells.	Serous, chief and parietal cells.	Columnar, mucous-albuminous.	Columnar and goblet.	Columnar and goblet.	Columnar and very many goblet.
Glands. {	Branched tubulo-acinar.	Branched tubular.	Branched tubular.	Convoluted tubular.	Branched tubulo-acinar.	Simple tubular.	Simple tubular.
	Mucosa and submucosa.	Mucosa.	Mucosa.	Mucosa.	Mucosa and submucosa.	Mucosa.	Mucosa.
Lymphatic nodules.....	Rare, small.	Many, medium.	Few, small.	Few, small.	Many, large, confluent.	Solitary and agminated.	Many, large, solitary.
Muscular coat.....	Striated or smooth.	Smooth.	Smooth.	Smooth.	Smooth.	Smooth.	Smooth.
Villi.....	None.	None.	None.	None.	Present.	Present.	None.

CHAPTER XVII

SALIVARY GLANDS AND PANCREAS

THE salivary glands include the smaller secreting glands of the oral cavity and three pairs of large compound tubulo-acinar glands, the parotid, submaxillary, and sublingual glands. All these are of the tubulo-acinar type, but certain ones secrete a mucous fluid while others produce an albuminous secretion which contains no mucous. The former are collectively known as the *mucous*, the latter as the *serous* salivary glands. Still other salivary glands secrete a fluid which is intermediate in composition, and as these glands contain certain alveoli which resemble those of the mucous, and others which are similar to those of the serous glands, this type is known as *mixed* salivary glands.

The salivary glands may therefore be subdivided into:

I. Mucous glands: sublingual, glands of Nuhn, and the mucous glands of the mucosa of the lips, cheeks, and tongue.

II. Mixed glands: submaxillary.

III. Serous glands: parotid, and v. Ebner's glands at the base of the tongue.

The form of the salivary glands will be appreciated by the accompanying diagram (Fig. 247) which represents one of the smaller glands of this

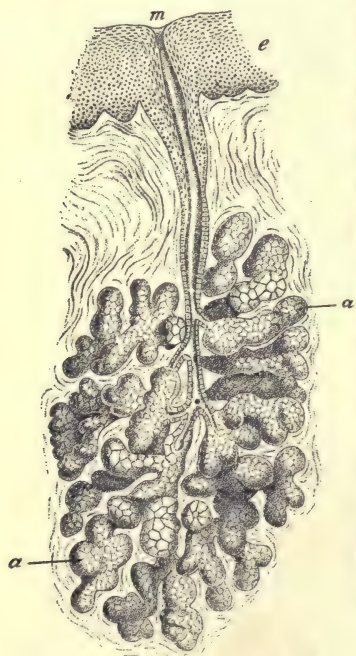


FIG. 247.—SEMIDIAGRAMMATIC REPRESENTATION OF A SMALL MUCOUS GLAND FROM THE ORAL MUCOSA OF A RABBIT.

a, mucous alveoli; *e*, epithelium of the oral mucosa; *m*, mouth of the glandular duct. $\times 70$. (After Kolliker.)

type. The larger ones are constructed in the same manner, the larger number of their secreting alveoli or acini arising through a more complex duct system.

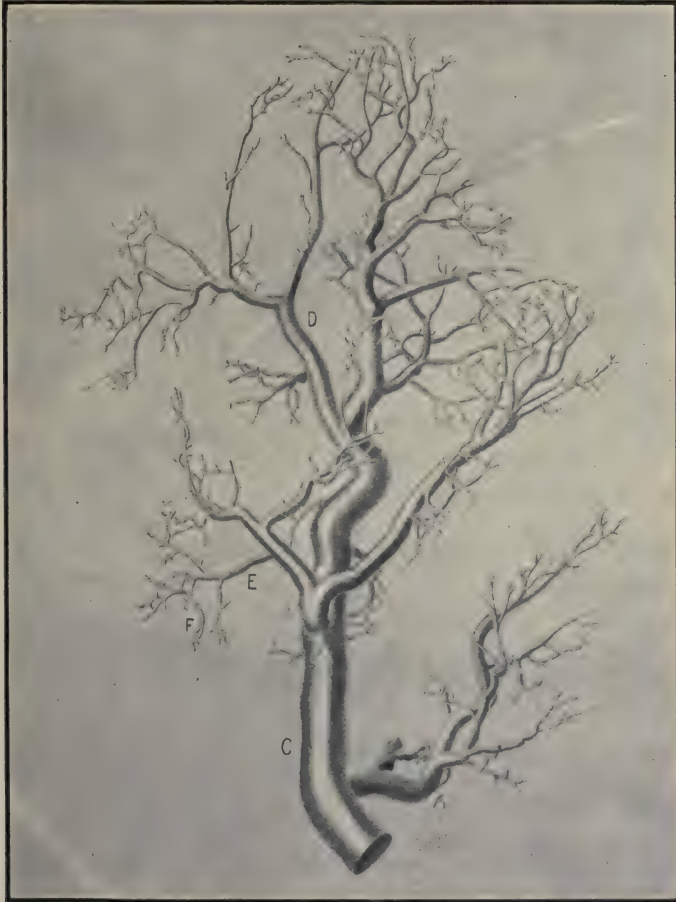


FIG. 248.—CORROSION MODEL OF AN INTERLOBULAR DUCT AND ITS BRANCHES, FROM THE HUMAN SUBMAXILLARY GLAND.

C, interlobular duct; *D*, large intralobular duct; *E*, small intralobular duct; *F*, intercalary duct. $\times 12$. (After Flint.)

The larger ducts of the gland are lined by columnar cells, which, as they approach their termination, become superposed and thus offer a gradual transition to the stratified epithelium upon whose surface they open. The epithelium rests upon a base-

ment membrane which, in the larger ducts, is invested with a fibro-elastic coat containing a few longitudinal smooth muscle fibres.

The ducts divide and subdivide in an arborescent manner, the larger branches lying in the connective tissue which invests the lobules into which the gland is subdivided, while the smaller branches are found within the lobule. The duct system is thus divisible into interlobular and intralobular ducts; the latter include the "salivary" and intercalary ducts.

In the smaller glands of the mouth the number of subdivisions of the duct system is relatively small, but in the larger salivary glands the small ducts are innumerable. Thus, in the submaxillary gland, Flint* found that the interlobular duct system formed 1,500 terminal branches, each of which entered a lobule and was further subdivided into intralobular and intercalary ducts before terminating in the secreting acini. The larger glands may therefore be said to bear to the smaller ones represented in Fig. 247, a relation which is comparable with that of a full-grown tree to the youngest sapling.

The smaller interlobular ducts are lined by columnar epithelium whose cells contain two zones, one on either side of the centrally situated nucleus. The distal zone or free extremity of the cell is finely granular, the proximal zone or base presents a characteristic striated appearance which is apparently due to a fibrillar structure of the cytoplasm in this portion of the cell. The epithelium is easily detached from its basement membrane by the artificial contraction of the tissues during fixation and hardening.

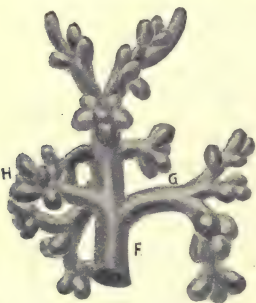


FIG. 249.—INTERCALARY DUCTS AND ACINI OF THE HUMAN SUBMAXILLARY GLAND, CORROSION MODEL.

F, small intralobular duct; G, intercalary duct; H, acini. Highly magnified. (After Flint.)

The lumen of the ducts is of considerable diameter and contains the reticulated or granular particles of the secretion. The larger ducts lie in the connective tissue septa which invest the lobular groups of acini. Each of these groups is derived from the ramifications of the terminal branch of an interlobular duct which enters the lobule to divide into numerous intralobular ducts, and secondarily, through a short intermediate or intercalary portion, into the

* Am. J. of Anat., 1902.

secreting alveoli or acini. The intercalary ducts are lined by low cuboidal epithelium and are the smallest tubules of the gland. As the duct passes into the acinus the tubule is increased in size, and its secretory epithelium becomes taller. The tubular acinus is more or less tortuous and possesses a sacculated or alveolar appearance.

The epithelium differs accordingly as it secretes a mucous or a serous fluid. Thus the acini are either mucous or serous secreting.

The **serous acini** contain pyramidal epithelial cells of sufficient height to almost completely fill the tubule; hence the lumen is

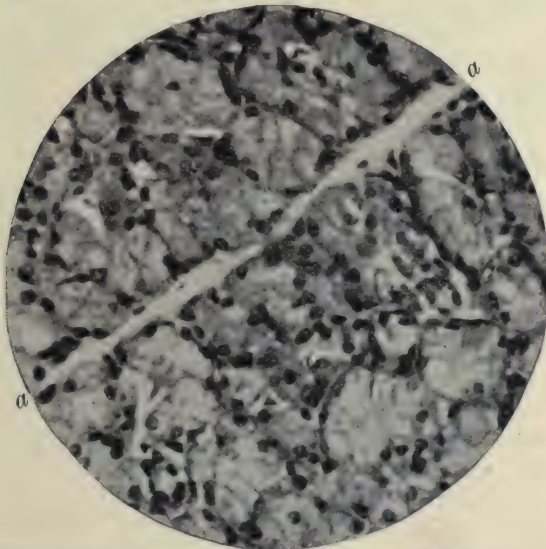


FIG. 250.—A GROUP OF SEROUS ACINI, FROM THE HUMAN SUBMAXILLARY GLAND.

a-a, interlobular connective tissue. Hematein and eosin. Photo. $\times 510$.

very narrow. The form of the secreting cells is somewhat irregular, a fact which apparently depends upon their crowded condition within the acinus. The nucleus is situated in the central portion or in the proximal end of the cell and is spheroidal in shape. The cytoplasm is finely granular, the granules being more prominent in the distal portion of the cell.

The epithelium rests upon a basement membrane within which, beneath the bases of the secreting epithelial cells, are certain flattened "*basket cells*" which here and there send short processes between the cells of the secretory epithelium and thus provide cup-

like depressions which receive the bases of the secreting cells. The function and origin of these "basket cells" is not at present known. They are readily recognized by their deeply stained and flattened nuclei which are contained within the thin cytoplasmic cell body.

The appearance of the secreting epithelium varies with its activity. During rest the granular secretion accumulates within the cell, until the non-granular zone is reduced to a narrow rim at its basal extremity and the nucleus is obscured and pushed somewhat basalward. The cell therefore becomes much swollen and the alveolar lumen almost obliterated. During activity the zymogen granules are discharged into the lumen, the cell shrinks and becomes clearer, the nucleus appears more distinct, and the granular zone becomes progressively narrower, the basal non-granular zone being correspondingly increased in breadth. In this basal zone elongated granules have been demonstrated, which are possibly to be regarded as prozymogen ("basal filaments" of Solger*).

The serous cells are provided with systems of secretory canaliculi which, beginning at the glandular lumen, invest the cell with a network of canals which lie in the intercellular substance and may even send short offshoots into the body of the cell itself. These canaliculi are considered to be characteristic of the serous acini and are not found in relation with the cells of the mucous acini (Fig. 252).

The mucous acini may contain only mucus secreting epithelium, or they may also include certain finely granular cells which resemble the epithelium of the serous glands. The former variety of acinus is found in the mucous glands at the base of the tongue and in the soft palate; the latter in the sublingual gland, in the glands of Nuhn, and in the mucous glands of the lips and cheeks.

The serous appearing cells of the latter form of mucous acinus are frequently arranged as crescentic groups bordering upon the adjacent mucous cells. Such groups are known as the *demilunes* of Haidenhain or *crescents* of Gianuzzi. They occur at the periphery of the acinus, their base being applied to the *membrana propria*, their inner margin sometimes reaching the glandular lumen, but more frequently separated therefrom by the overlapping of the adjacent mucus cells. The *demilunes* are frequently found at the blind extremity of the secreting acinus, but they may also occur along its sides.

* Festschr. f. C. Gegenbaur, 1896.

The nature of the demilunes is the subject of considerable discussion. Haidenhain * first advanced the theory that the mucous cells were destroyed during secretion, and that the function of the demilunes was therefore to replace the disintegrated mucinous

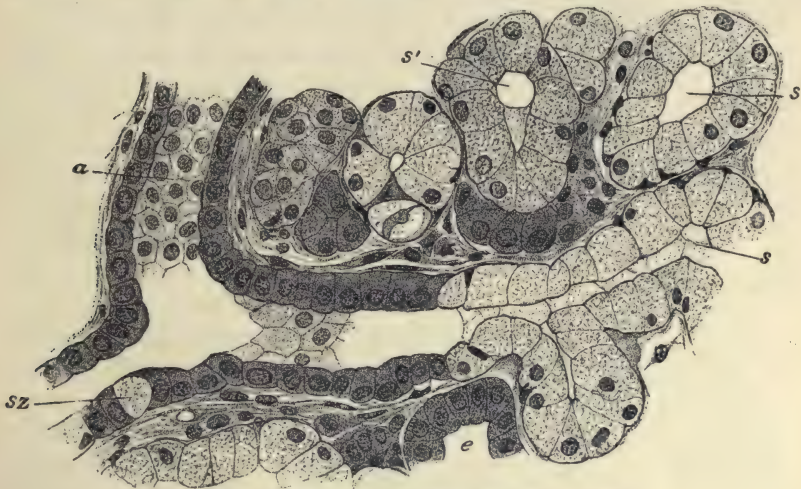


FIG. 251.—FROM THE SUBLINGUAL GLAND OF MAN.

a, intralobular duct; *e*, acinus whose cells contain no mucus; *s*, mucous acini, at *s'* with a demilune; *sz*, mucous cells in the duct. $\times 500$. (After Kölliker.)

cells. This theory has been practically abandoned, for no one has yet demonstrated active cell division in the demilunes, a process which would necessarily be concomitant with the rapid development of mucous from demilune cells.

Hebold † is responsible for the theory, strongly supported by Stöhr, that the demilunes represent an inactive, the mucous cells an active phase of mucous secretion. The easy demonstration of intermediate stages in many mucus secreting glands lends strong support to this theory, and in the present state of our knowledge it seems beyond doubt that such a process actually occurs in at least some of the mucus secreting glands.

A third theory, more recently advanced by Solger ‡ and stoutly supported by Krause § and others, considers the demilunes to be true secreting cells which form a serous secretion and are therefore functionally independent of the mucinous cells. This theory

* Arch. f. mik. Anat., 1869.

† Anat. Anz., 1894.

‡ Bonn, 1879.

§ Arch. f. mik. Anat., 1895, 1897, and 1901.

receives strong confirmation in the fact first observed by Cajal * and since that time repeatedly demonstrated, that the demilunes, like the true serous cells, are provided with



FIG. 252.—MUCOUS ACINI OF THE RETROLINGUAL GLAND OF THE RAT.

The ducts and secretory capillaries have been blackened. *r*, demilunes with secretory capillaries; *s*, mucous cells. Golgi method. $\times 500$. (After Kölliker.)

a system of intercellular secretory canaliculi by which they are placed in relation with the glandular lumen. Moreover Krause was able to demonstrate that granules of sodium indigo-sulphate were secreted by these cells, as also by the true serous cells and the striated epithelium of the intralobular ducts.

The mucus secreting cells examined in the fresh state present a clear highly refractive appearance. They closely resemble the typical goblet cells, but instead of being isolated among the granular serous cells, they may invest the entire acinus, or even the whole of a small lobule may contain only mucus secreting cells.

After the customary preparation by fixation and staining, the mucous cells present a coarse basophilic reticulum which occupies the distal portion of the cell. Coarse granules,

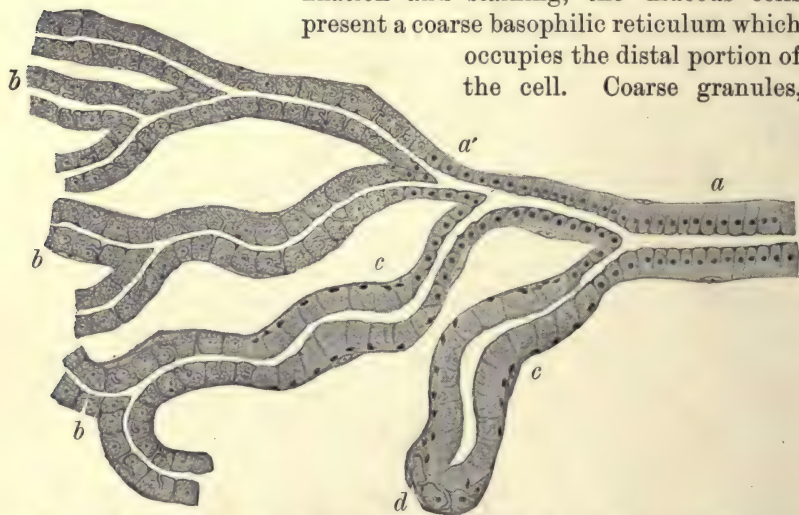


FIG. 253.—DIAGRAM OF THE ARRANGEMENT OF THE CELLS IN A MIXED SALIVARY GLAND. *a*, intralobular duct; *a'*, intercalary duct; *b*, serous secreting tubules; *c*, mucus secreting tubules; *d*, demilune. (After Krause.)

* Barcelona, 1889.

with proper fixation, and in fresh tissue as well, can be demonstrated within the meshes of the reticulum. These granules are readily colored by the so-called specific mucin stains (Mayer's muchematein and mucicarmine, safranin, and thionin).

In the mucous cells the nucleus is crowded to the base or proximal end of the cell and flattened against the basement membrane. It is surrounded by a small remnant of finely granular cytoplasm, which, after the discharge of the mucus during secretion, is presumably capable of reloading the cell with its *mucinous content*.

We will now consider the more important peculiarities of each of the larger salivary glands.

THE PAROTID GLAND.—This is, in man,* the largest of the salivary glands and is purely a serous secreting organ. The lobules of the parotid are firmly united by dense but narrow bands of connective tissue which contain the larger ducts, blood vessels, lymphatics, and a few small ganglia.

The secreting acini are relatively long and tortuous; they are frequently branched or forked. Because of the relatively low height of their serous secreting cells the acini

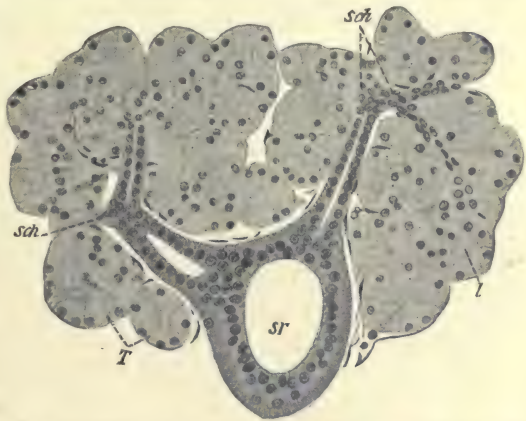


FIG. 254.—FROM A SECTION OF THE HUMAN PAROTID GLAND.

l, lumen of a serous acinus; sch, intercalary duct; sr, intralobular duct; T, secreting acini. Hematoxylin and eosin. $\times 280$. (After Sobotta.)

appear slender and their lumen is irregular, indistinct, and very narrow. The "basket cells" upon which the secreting cells rest are highly developed in the parotid and often form a complete investment for the acinus.

The acini of the parotid are all of one type. The only other tubules within the lobules of this gland are the intercalary and the intralobular or *salivary* ducts. The former are characterized

* In the dog and a few other mammals the parotid has a mucinous secretion.

by their very narrow caliber and low epithelium. They are slender tubules which open on the one side *from* the acini and on the other *into* the branched terminals of the salivary ducts. In the parotid the salivary ducts are relatively short as compared with the other salivary glands, but are readily recognized by their striated columnar epithelium, which is deeply colored by acid dyes (eosin, etc.) and are thus sharply distinguished from the secreting cells, which stain poorly with these dyes.

THE SUBMAXILLARY GLAND.—In man and in most mammals this organ is a mixed salivary gland; that of the bear and dog contains the largest, that of man and the apes the smallest proportion of mucus acini (Krause).*

The serous acini of the submaxillary are shorter and less typically tubular than those of the parotid, and they are lined by taller secreting cells. The diameter of the acinus is therefore slightly greater in this gland than in the parotid. Its mucous acini contain a relatively large proportion of demilunes.

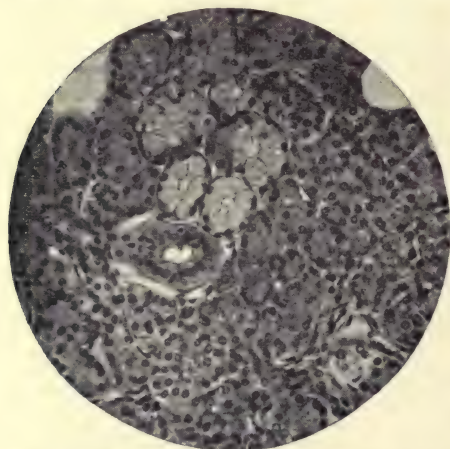


FIG. 255.—FROM A SECTION OF THE HUMAN SUBMAXILLARY GLAND.

In the centre is a small salivary duct, just above which are three mucous acini, the uppermost one possessing a demilune. The other acini are serous. Hematein and eosin. Photo. $\times 370$.

The intercalary ducts are still shorter than in the parotid while the intralobular ducts are more prominent in the submaxillary. The interlobular connective tissue is not quite so fine as in the parotid. It contains many sympathetic ganglia of relatively large size. Small Pacinian corpuscles of simple construction are

occasionally found in the interlobular connective tissue (Krause).

THE SUBLINGUAL GLAND.—This is a mucus secreting gland, all of whose acini contain mucous cells though they also contain very many demilunes (serous cells), so that although isolated sections which pass through the larger collections of demilune cells may appear as sections of serous secreting tubules, yet, if examined

* Arch. f. mik. Anat., 1897.

in longitudinal section or by reconstruction, the true mucous character of each lobule is apparent. Many of the terminal acini of the sublingual gland, however, although much branched, contain

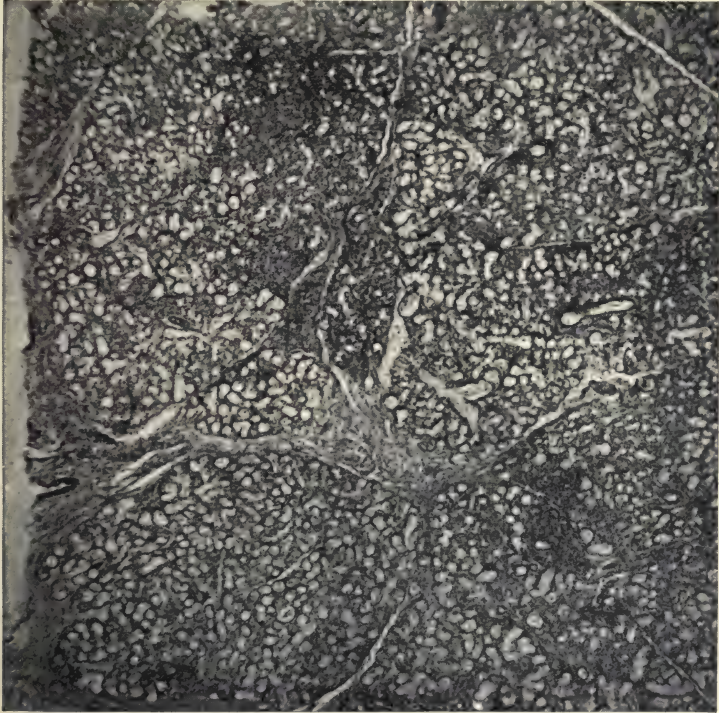


FIG. 256.—FROM A SECTION OF THE SUBLINGUAL GLAND OF MAN; THE LIGHTER AREAS ARE THE MUCOUS ACINI.

Hematein and eosin. Photo. $\times 53$.

no demilunes. The “basket cells” are readily recognized in the acini of this gland though they are less highly developed here than in the parotid.

Blood Supply.—The salivary glands possess a rich blood supply. The arteries accompany the glandular ducts within the interlobular connective tissue, and thus reach all the lobules of the gland. Small arterial twigs enter the lobule from all sides and form a rich capillary plexus in the delicate connective tissue coats of the acini. The capillaries are thus brought into intimate relation with the secreting cells, from which they are only separated by the basement membrane of the acinus. The veins return by a similar

course, the smallest venules passing out of the lobule into the connective tissue septa in which they retrace the course of the arteries.



FIG. 257.—RECONSTRUCTION MODEL OF THE SUBLINGUAL GLAND OF MAN.

An intralobular duct terminating in intercalary ducts and acini. $\times 285$. (After Maziarski.)

illary and least numerous in the parotid gland.

Delicate fibre bundles from the interlobular nerve trunks enter the lobules and form a plexus of naked fibrils about the walls of the acini, known as the *epilemmal plexus*, from which terminal fibrils pierce the basement membrane and as *hypolemmal fibres* end in contact with and between the secreting cells. Small terminal expansions, varicosities, or end knobs are found in the course of the hypolemmal fibres.

THE PANCREAS

The pancreas bears a close structural resemblance to the salivary glands. It is a compound tubulo-acinar gland which contains an immense number of small lobules and which pours its secretion into the lumen of the duodenum by means of the pancreatic ducts

Lymphatics are relatively few and are for the most part confined to the interlobular septa, where they form cleft-like spaces which lead to true lymphatic vessels and so on to the lymphatic glands of the cervical region.

Nerve Supply.—The salivary glands are abundantly supplied with nerves, which are derived from both sympathetic and cerebro-spinal trunks. They are distributed to the walls of the blood vessels and ducts, and to the secreting cells of the acini. The nerve trunks are found in the interlobular connective tissue where they are supplied with small ganglia which are most abundant in the submax-

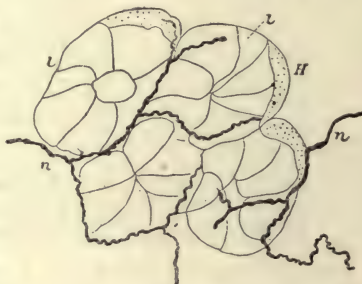


FIG. 258.—NERVE ENDINGS IN A SALIVARY GLAND.

H, demilune; l, secreting acini; n, nerve fibrils. Highly magnified. (After Retzius, from Rauber.)

of Wirsung and Santorini. The lobules are united by a delicate and relatively very loose connective tissue.

The ducts of the pancreas branch and arborize in the same manner as those of the salivary glands. The interlobular ducts

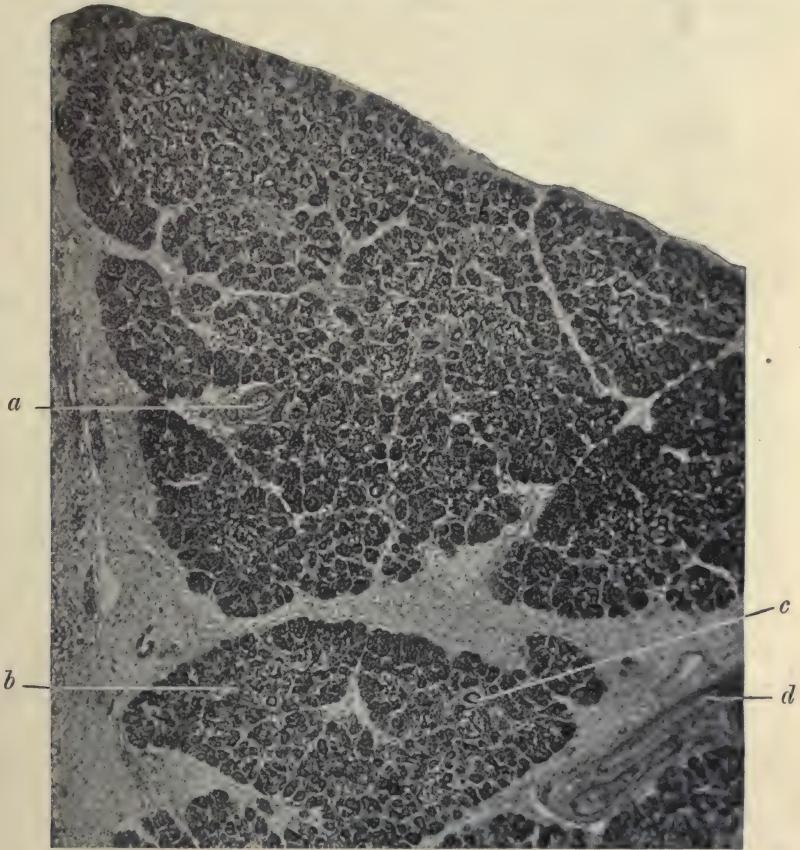


FIG. 259.—FROM A SECTION OF THE HUMAN PANCREAS, SHOWING SEVERAL LOBULES AND THE BROAD INTERLOBULAR BANDS OF CONNECTIVE TISSUE.

a, blood vessel; *b*, island of Langerhans; *c*, intralobular duct; *d*, interlobular duct and accompanying artery. Hematein and eosin. Photo. $\times 45$.

are lined by a single layer of columnar cells; in the larger divisions occasional goblet cells are found. The wall of the interlobular pancreatic ducts is much thicker than in those of the salivary glands, for they possess a much thicker connective tissue coat, in which are also many longitudinal smooth muscle fibres.

On entering the lobule the duct is immediately transformed into the intercalary type; in the pancreas there are no intralobular ducts lined by columnar striated epithelium as in the salivary glands. The intercalary ducts are very slender tubules which are lined by low columnar or flattened epithelium. Because of the absence of larger intralobular ducts the intercalary portions are relatively very long and much branched.



FIG. 260.—RECONSTRUCTION MODEL OF THE HUMAN PANCREAS.

The intralobular duct gives off long intercalary ducts, which, after branching, end in the acini. $\times 344$. (After Maziarski.)

On approaching its termination the lining cells of an intercalary duct are still more flattened and often acquire a considerable breadth. They pass into the acini in a peculiar manner. Instead of offering a direct transition from the duct epithelium to that of the acinus the cells of the former frequently appear as if telescoped into the lumen of the acinus. Thus the **centro-acinar cells** of Langerhans are produced, and consequently the centro-acinar cells correspond closely in appearance with those of the intercalary ducts. They seem to occupy the lumen

of the acinus, and are only separated from the distal ends of the acinar cells by the secretory capillaries which place the secreting cells in communication with the lumen of the duct. The centro-acinar cells are characteristic of the pancreatic acini.

THE ACINI of the pancreas possess an irregular tubular form with frequent alveolar dilatations. Their lining epithelium rests upon a reticular basement membrane within which are thin "basket cells." A delicate connective tissue stroma invests the acini.

The secreting cells are tall and irregularly columnar or pyramidal in shape. Their nucleus lies in the proximal third of the cell and is surrounded by reticular or very finely granular cytoplasm. The cytoplasm of the inner zone of the cell, on the other hand, is filled with coarse zymogen granules whose number is dependent upon the activity of the gland. During fasting the granules accumulate until eventually they almost completely fill

the cell, but during digestion they disappear with the discharge of the secretion, the width of the granular zone gradually decreasing, that of the non-granular basal zone being correspondingly enlarged.

With the increased breadth of the basal zone during secretion, there appears in this portion of the cell a structure which has been described by Nussbaum * as the *Nebenkern*, and which has been

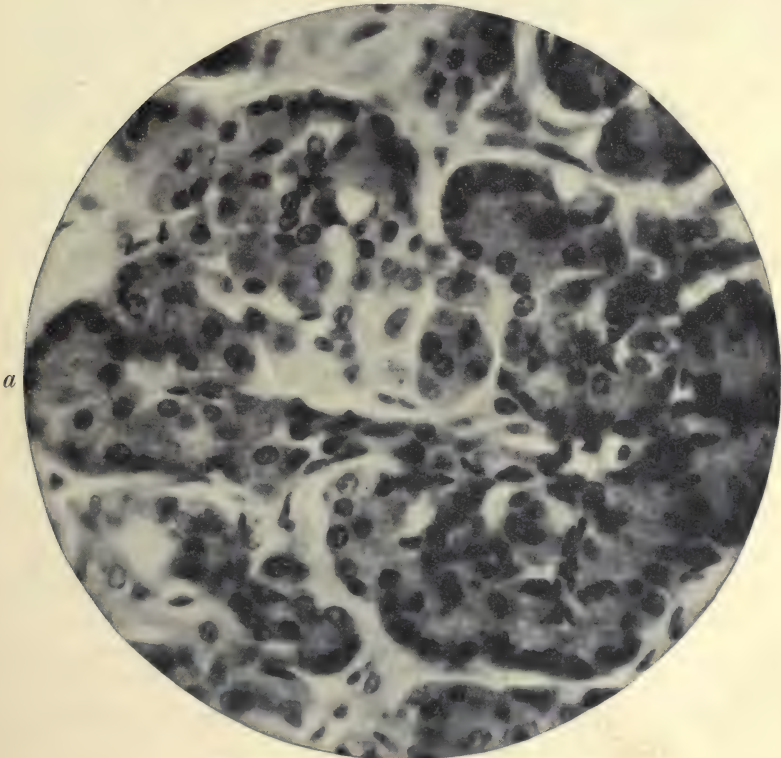


FIG. 261.—ACINI OF THE HUMAN PANCREAS.

The acinus at *a* is connected with an intercalary duct, cut in tangential section, and occupying the center of the figure. Hematein and eosin. Photo. $\times 950$.

carefully studied by Mathews.† This is a spheroidal basophile body which lies near the nucleus and is frequently surrounded by a clear area of cytoplasm. Its origin and function are somewhat doubtful and it is possible that several distinct bodies have been

* Arch. f. mik. Anat., 1885.

† J. of Morph., 1899.

included under this name. Ogata* considers that it is derived from the nucleus by the extrusion of its plasmosome, an opinion which seems to be shared by von Ebner.† The studies of

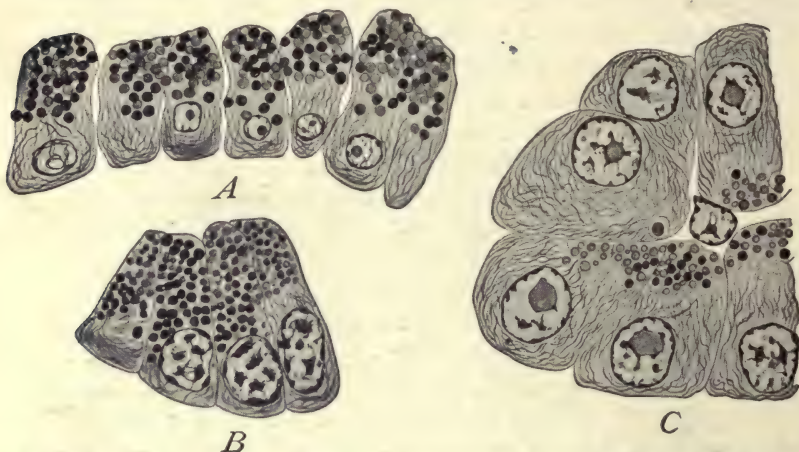


FIG. 262.—CELLS FROM THE PANCREAS OF NECTURUS IN VARIOUS STAGES OF SECRETION. *A* and *B*, show the appearance of cells which are nearly filled with secretion after a period of rest; *C*, after active secretion. Highly magnified. (After Mathews.)

Mathews, however, show that at least in certain instances it is distinctly fibrillar and that it is concerned with the mechanism of secretion (see Fig. 3, page 3).

ISLANDS OF LANGERHANS.—Most of the lobules of the pancreas contain, in addition to the acini and ducts, certain minute collections of spheroidal or polyhedral cells which lie in the inter-acinar connective tissue and which, though they possess the appearance of secreting cells, are in no way connected with the duct system. These cell groups are known as the *islands of Langerhans* (*intralobular cell groups*). They are most abundant in the splenic end of the gland (Opie).‡

The insular cells form a spheroidal group which is abundantly supplied with blood capillaries. Occasionally the cells form columnar strands between the capillary vessels but more frequently they are irregularly disposed. Still more rarely they are so grouped about a capillary vessel as to give a false impression of a tubular structure. These cells possess a finely granular or reticular cytoplasm and a central spheroidal nucleus. It is supposed

* Arch. f. Physiol., 1883.

† Kölliker's Handbuch 1902, Bd. iii, S. 250.

‡ Johns Hop. Hosp. Bull., 1900.

that they form an internal secretion which enters the blood vessels and exerts an influence upon carbohydrate metabolism.

Ontogenetically the islands of Langerhans are derived from the tubular acini but are separated therefrom during the third month of fetal life (Pearce). * In the adult they appear to have no connection whatever with the acini. In perfectly impregnated specimens prepared by Dogiel † by the method of Golgi, no secre-

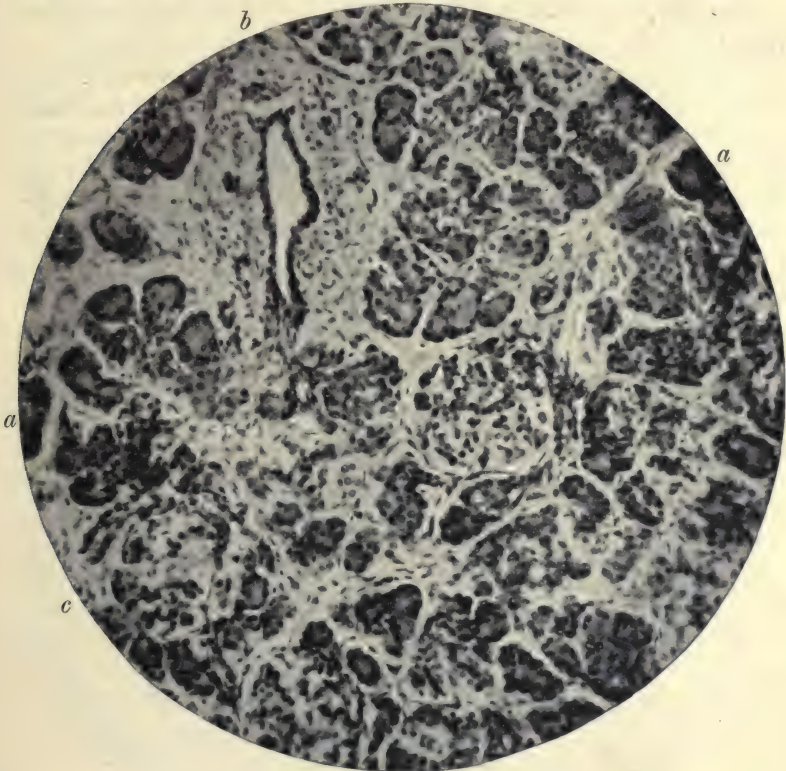


FIG. 263.—FROM THE HUMAN PANCREAS.

a, acini; *b*, is placed above an interlobular duct; *c*, an island of Langerhans; a second island, circular in outline, lies near the center of the figure. Hematein and eosin. Photo. $\times 330$.

tory capillaries could be demonstrated connecting the cells of the islands with the lumen of the acini.

Blood Supply.—The large blood vessels of the pancreas accompany the interlobular ducts, but after repeated subdivision these

* Amer. J. of Anat., 1903.

† Arch. f. Anat., 1893.

vessels part company and the smaller arteries pursue a separate course through the interlobular connective tissue. Thus they reach all portions of the gland and supply capillaries to the intralobular connective tissue about the acini. Certain arterial branches also enter the islands of Langerhans and form a specially rich plexus of broad capillaries within these cell groups. The veins return by a similar course.

The lymphatics are mostly confined to the interlobular tissue, where they are in relation with the blood vessels.

The nerves are derived from the sympathetic, and occur as small trunks within the interlobular connective tissue. Numerous small ganglia occur in their course. As in the salivary glands the nerves supply the vascular walls. About the secreting acini they form a delicate network of naked fibrils from which end branches penetrate the basement membrane and terminate upon the secreting cells. Pacinian corpuscles are occasionally found in the interlobular connective tissue of the pancreas.

Resumé.—Finally the attention of the student should be specially directed to the presence of the islands of Langerhans, the centro-acinar cells, the very distinct inner and outer zones of the secreting cells, the thick walls of the interlobular ducts, the absence of intralobular ducts except of the intercalary type, and the loose character of the interlobular tissue as the distinguishing characteristics of the pancreas.

CHAPTER XVIII

THE LIVER

THE liver is the largest secreting gland of the body, and may be classed as a peculiar form of compound tubular gland whose

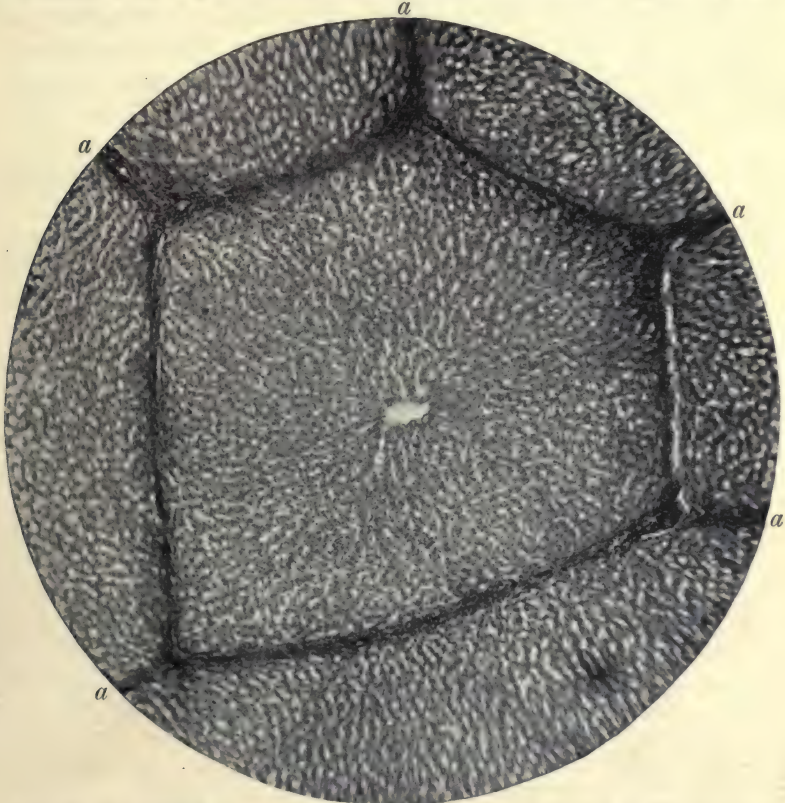


FIG. 264.—A LOBULE OF THE PIG'S LIVER; THE CENTRAL VEIN LIES IN THE MIDDLE OF THE FIGURE.

a, capsule of Glisson. Hematein and eosin. Photo. $\times 115$.

cells resemble the serous secreting type. The organ is invested with a connective tissue sheath the greater portion of which is

clothed with peritoneal epithelium. From this connective tissue capsule, fibrous bands or septa are continued into the substance of the organ and permeate to all its portions. These processes of connective tissue, collectively forming the *capsule of Glisson*, are most abundant at the transverse fissure, where they contain the large blood vessels and hepatic ducts, this fissure serving as a hilum for the organ.

The liver is dependent for its structural peculiarities upon the peculiar disposition of the connective tissue of Glisson's capsule, as also of the blood vessels whose branches it contains, for by these tissues the substance of the liver is extensively subdivided into minute collections of hepatic cells, each group forming an anatomical unit, the *hepatic lobule*, which in addition to the hepatic cells contains a connective tissue reticulum and the smaller blood vessels and secretory capillaries (bile canaliculi). The hepatic lobules are analogous to the lobules of compound tubulo-acinar glands, inasmuch as they contain the secreting parenchyma of the organ, but are very different from the latter in the arrangement of the secreting cells which, in the human liver, do not present either a tubular or acinar structure, but form more solid cell columns.

Thus in the human liver the tubular character of the gland is scarcely apparent, yet in the liver of many of the lower animals, notably in that of the turtle and frog, the cells form typical tubules within the indistinct hepatic lobules.

The bile formed by the liver cells is conveyed to the duodenum by an excretory system, beginning with innumerable interlobular bile ducts which receive the intralobular secretory capillaries, and, leaving the lobule from all its sides, find their way through the interlobu-

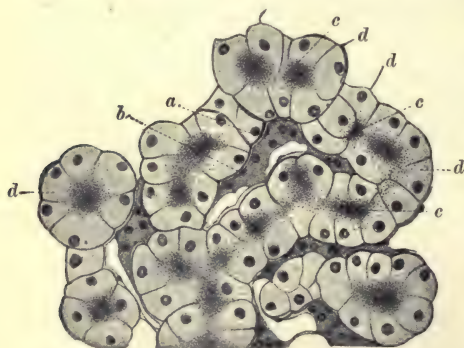


FIG. 265.—FROM A SECTION OF THE TURTLE'S LIVER, SHOWING THE TUBULAR ARRANGEMENT OF THE PARENCHYMA.

a, blood capillary, partially filled with clotted blood; *b*, vascular endothelium; *c*, darkened central portions of the hepatic cells; *d*, peripheral portion of the hepatic cells. Osmium tetroxid; carmin. $\times 400$. (After Shore and Jones.)

lar connective tissue of the capsule of Glisson, unite with their fellows to form larger and larger bile ducts, and finally leave the

organ at the hepatic duct, thus reaching the gall bladder and intestine by means of the cystic and common bile ducts. In all their course the bile ducts are in close relation with the radicals of the portal vein and of the hepatic artery, the group of vessels forming the so-called *portal canals*.

THE HEPATIC CONNECTIVE TISSUE.

—The hepatic connective tissue, or the supporting tissue of the liver, includes the capsule of the organ and the capsule of Glisson, —the latter forming a framework

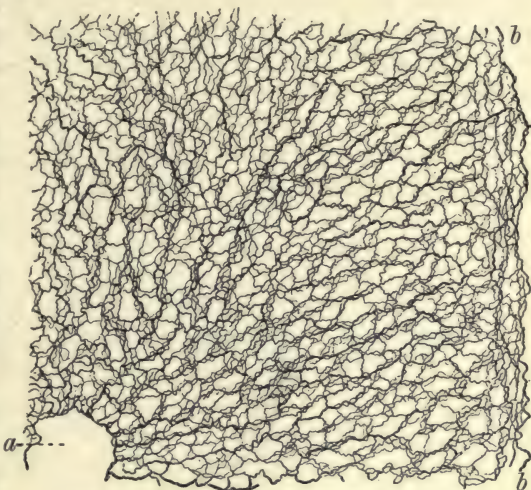


FIG. 266.—THE RETICULUM OF THE DOG'S LIVER.

a, central vein; *b*, capsule of Glisson at the margin of the lobule. Gold chlorid. $\times 120$. (After Böhm and von Davidoff.)

throughout the liver and inclosing its hexagonal lobules—together with the more delicate intralobular reticulum. These tissues convey the blood vessels, lymphatics, nerves, and bile ducts.

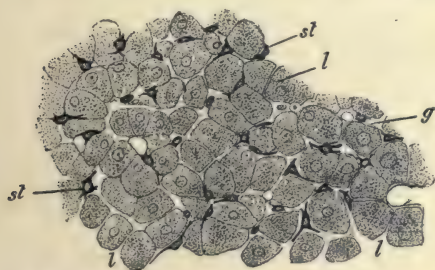


FIG. 267.—STELLATE CELLS OF VON KUPFER IN THE LIVER OF A DOG.

g, capillary blood vessel; *l*, hepatic cells; *st*, stellate cells. Gold chlorid. $\times 200$. (After Kölliker.)

The fibrous framework, which forms both the outer fibrous capsule of the liver and the capsule of Glisson, contains both fibrous and elastic tissue, the latter being fairly abundant, a fact which sharply contrasts with the complete absence of elastic fibres from the interior of the hepatic lobules.

The intralobular connective tissue is extremely delicate, and consists of very fine fibrils and stellate cells (von Kupfer) which form a delicate reticulum in which the capillary blood vessels and

columns of liver cells are suspended. The anastomosing strands of reticulum converge from the periphery toward the center of the lobule, thus following the course of the blood capillaries and cell columns. This reticular tissue (Mall) exists in so small a quantity and is so extremely delicate that although it can be readily studied after removal of the liver cells, as by artificial digestion, in ordinary preparations, except those of extreme thinness, it can scarcely be discovered in the minute clefts between the cell columns and the blood capillaries.

The volume of the interlobular connective tissue which forms Glisson's capsule varies greatly in different animals. In the liver of the pig this tissue is very extensive and forms a complete investment for each lobule. In man it is very limited in amount and is confined to minute areas between the adjacent angles of the lobules, with an occasional fragment separating the lateral surfaces of neighboring lobules. It is in the latter portions, viz., between the opposed surfaces of the lobules, that the branches of the hepatic veins (sublobular veins) are found. The interlobular veins, the subdivisions of the portal vein, together with the bile ducts and the branches of the hepatic artery are found at the angles of adjacent lobules; hence the portal canals, which contain these vessels, should always be sought in this location, while the sublobular veins, which run alone and form no part of the portal canals, will be found between the opposed surfaces of the lobules.

The capsule of Glisson also contains many lymphatic vessels and non-medullated nerve fibres.

THE HEPATIC LOBULE.—The lobule is the structural unit of the liver and consists chiefly of hepatic cells which are arranged in radiating columns. In shape the lobule is an irregularly hexagonal pyramid, the exact number of its faces being extremely variable. The periphery of the lobule is outlined by the connective tissue of Glisson's capsule which either completely invests each lobule, as in the pig's liver, or forms only a very incomplete investment, as in the liver of man.

Blood enters the lobule from the vessels of the portal canals and finds its way, through converging capillaries, from the periphery to the center of the lobule. Here it enters the intralobular or central vein, which occupies the axis of the lobule and conveys the blood thence to the sublobular veins, which again lie in the interlobular connective tissue of Glisson's capsule.

The hepatic cells occupy the meshes of the intralobular capillaries and are arranged in columns which radiate from the central vein toward the periphery. The frequent anastomoses of the capillaries as they approach the central vein produce great irregularities in the arrangement and length of the cell columns. Each

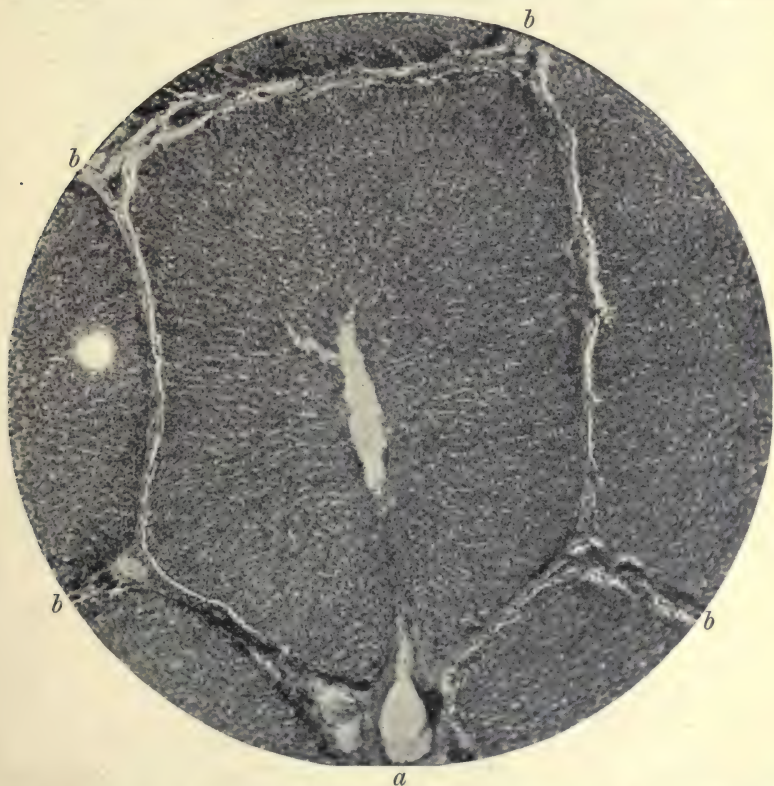


FIG. 268.—A LOBULE OF THE PIG'S LIVER IN LONGITUDINAL SECTION, SHOWING THE RELATION OF THE CENTRAL AND SUBLOBULAR VEINS AND THE ARRANGEMENT OF THE HEPATIC CELLS.

a, sublobular vein; *b*, capsule of Glisson. Hematein and eosin. Photo. $\times 68$.

column, however, reaches the periphery of the lobule after a more or less tortuous course, and it is here that the secretory bile capillaries, which are found within the cell columns, become continuous with the minute bile ducts of the portal canals.

The bile capillaries occur as secretory canaliculi between the opposed surfaces of the hepatic cells. They are thus found with-

in the cell columns and stand in the same relation to the hepatic cells as though each cell column formed a tubule whose capillary lumen, the bile canaliculus, was surrounded by only two secreting cells, whereas in other tubular glands a larger number of cells encircle the lumen of the secreting tubule. Hence the bile capillaries and the blood capillaries are never in contact, but are always separated by at least one-third to one-half the diameter of a hepatic

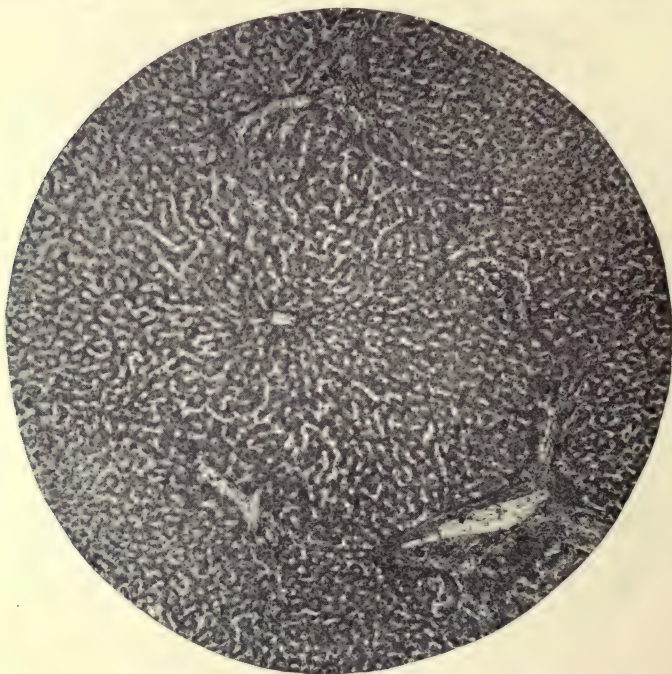


FIG. 269.—A LOBULE OF THE HUMAN LIVER, SEEN IN TRANSECTION.

It is outlined by three small portal canals and contains a single central vein. Hematein and eosin. Photo. $\times 50$.

cell. The bile capillary occurs on that surface of the hepatic cell which is in contact with other cells within the column; the blood capillary, on the other hand, is in relation with that surface of the hepatic cell which forms the periphery of the cell column.

The blood capillaries are suspended in the fine meshes of the delicate reticulum which has already been described as the intra-lobular connective tissue, and which also invests the columns of hepatic cells. This connective tissue is of relatively insignificant volume.

The bile capillaries are true secretory canaliculi by which the bile, after secretion by the hepatic cells, finds its way along the

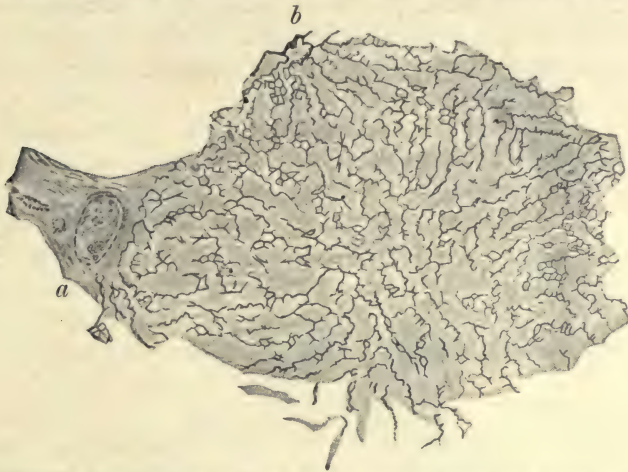


FIG. 270.—BILE CAPILLARIES OF THE HEPATIC LOBULE, FROM THE LIVER OF A CAT. *a*, a portal canal; *b*, a small interlobular bile duct. Golgi's stain and hematein. Moderately magnified. (After Geberg.)

anastomosing cell columns to some point at the periphery of the lobule, where the cell column becomes continuous with a minute bile duct, the secreting cells within the lobule presenting a rapid

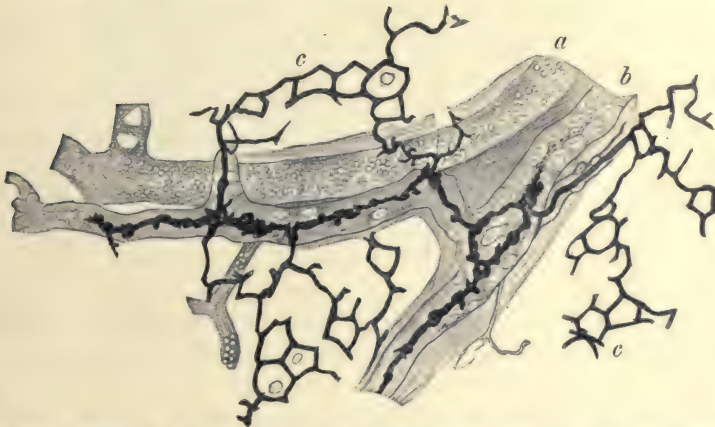


FIG. 271.—SHOWING THE CONNECTION BETWEEN THE INTRALOBULAR AND INTERLOBULAR BILE DUCTS IN THE CAT'S LIVER.

a, interlobular vein; *b*, interlobular bile duct; *c*, intralobular bile capillaries. Golgi stain and hematein. Highly magnified. (After Geberg.)

transition to the very low columnar or flattened epithelium of the interlobular bile duct.

THE HEPATIC CELLS.—These are large polyhedral cells which possess one, or very frequently two, spherical nuclei and a coarsely granular cytoplasm. A true cell membrane may be regarded as being absent, yet there is often a sharply defined exoplasm which forms the surface of the cell and simulates a true membrane.

The nuclei of the hepatic cells are rich in chromatin, and stain deeply. They are situated well within the cell, but usually in an eccentric position. Frequently they contain a distinct nucleolus.

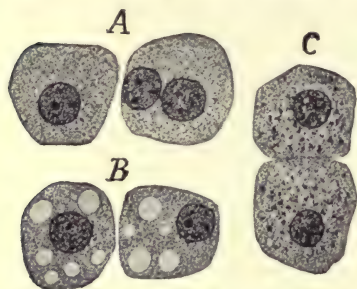


FIG. 272.—TYPES OF CELLS FROM A SECTION OF THE NORMAL HUMAN LIVER.

A, the usual type of liver cell; *B*, fatty, and *C*, pigmented cells. Types *B* and *C* were very scarce. Hematein and eosin. $\times 900$.

The cytoplasm of the hepatic cell is finely reticular, the meshes being filled with coarse granules of irregular size. Many of these are undoubtedly *glycogenic* granules, and show a decided reaction when acted upon by Lugol's solution of iodine after alcoholic fixation. The amount of glycogen present varies with the diet. After digestion and absorption of a carbohydrate meal it is greatly increased, but disappears during

fasting. Even when glycogen is quite deficient, the hepatic cells still present a granular appearance from the presence of other substances, possibly *zymogens*.

Fat globules occur in the hepatic cells in limited numbers, and appear to be a normal constituent. The globules vary much in size, but are all very small. Their number is also dependent upon diet and digestion. During absorption of a fatty meal, fat globules occur in considerable numbers, and are most numerous in those hepatic cells which are at the periphery of the lobule. They are not normally found in the vicinity of the central vein.

The hepatic cells also frequently contain brown or yellowish-brown granules of ferruginous *pigment*, which are more prone to occur in the interior of the lobule near the central vein. When present in considerable amount this pigment can no longer be considered a normal constituent of the hepatic cell.

THE PORTAL CANALS.—The portal canals are formed by the ramifications of the portal vein, hepatic artery, and hepatic

duct, and are characteristic of the liver, the peculiarity consisting not so much in the structure of the tissue, as in the combination of artery, duct, and vein occurring in close relation, in the connective tissue at the angles of the hepatic lobules. The largest vessel in the canal is invariably the vein, the smallest the artery.

The Interlobular Veins, branches of the portal, are extremely thin-walled vessels. They are formed by scarcely more than the endothelial lining, which is supported by the connective tissue of Glisson's capsule. Their wall contains very little or no smooth muscle.

The Interlobular Arteries, branches of the hepatic, are very small and are noted for their highly developed muscular coat and distinct elastic membrane. They give off minute vaginal branches which supply capillaries to the tissue of Glisson's capsule.

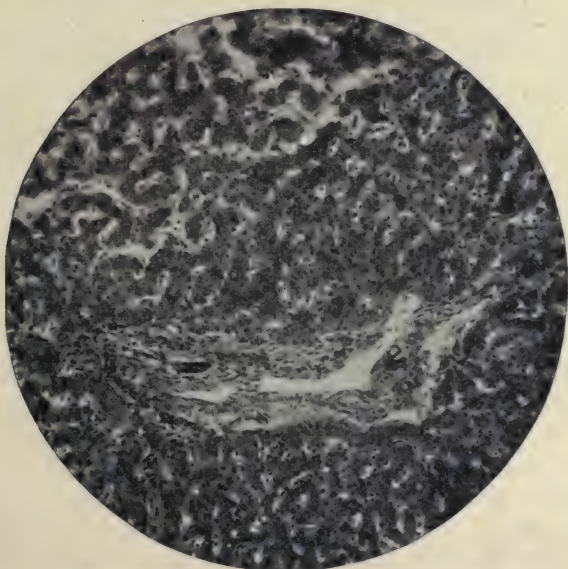


FIG. 273.—A PORTAL CANAL OF THE HUMAN LIVER.

The large thin-walled vessel in the center of the connective tissue is the interlobular vein; at its left are two ducts in oblique and longitudinal section; at the right of the vein, a duct and an artery are seen in transection. Hematein and eosin. Photo. $\times 375$.

The Interlobular Ducts, radicals of the hepatic duct, receive the bile from the intralobular bile canaliculi and convey it, through larger and larger branches, to the hepatic duct. They are more numerous than the interlobular veins and much more numerous

than the interlobular arteries. The ducts are lined by columnar epithelium whose height varies with the size of the tubule, the smallest ducts being lined by low columnar or cuboidal, the largest by tall columnar cells; the lining epithelium of the hepatic and common bile ducts is very tall. The epithelial cells of the ducts possess characteristic spherical or ovoid nuclei which are heavily loaded with chromatin. Their cytoplasm is clear or finely reticular. The largest ducts contain a few goblet cells; small mucous glands are found in the hepatic and common bile duct.

The epithelium of the interlobular bile ducts rests upon a thin basement membrane, which is surrounded by a thick fibro-elastic coat. The larger ducts are also supplied with circular smooth muscle fibres, which, in the largest branches, form a considerable coat (Fig. 239, page 293). Outside of the liver longitudinal muscle fibres also appear in the walls of the excretory ducts, and so accumulate in the wall of the gall bladder and common bile duct as often to form a distinct layer.

BLOOD SUPPLY.—The liver is supplied with blood from two independent sources, the hepatic artery and the portal vein. That supplied by the artery is of minor importance and is destined only for the nutrition of the connective tissue framework of the organ.

On entering the liver at the transverse fissure the **hepatic artery** gives off numerous capsular branches which ramify in the capsule of the liver and supply capillaries to its connective tissue. Other branches, the direct continuation of the hepatic artery, enter the portal canals and by repeated division form the *interlobular arteries*, which ramify in the tissue of Glisson's capsule, and whose vaginal branches supply capillaries to this connective tissue. These capillaries, as well as those from the capsular branches, become continuous, at the periphery of the lobule, with the intralobular capillaries which are derived from the branches of the portal vein.

The **Portal Vein** likewise enters at the transverse fissure, bringing to the liver the blood collected from the capillaries of the organs of digestion and absorption. It divides into numerous branches which follow the portal canals, in which they are known as the *interlobular veins*, and in this way reach all portions of the organ.

The interlobular veins throughout all their course give off small branches which at once enter the periphery of the hepatic lobules and immediately break into a brush of capillary vessels.

These *intralobular capillaries* converge toward the center of the lobule and anastomose to form a capillary network, in the elongated meshes of which are the columns of hepatic cells. These capillaries approach the center of the lobule where they unite to form the intralobular or central vein. The central vein frequently

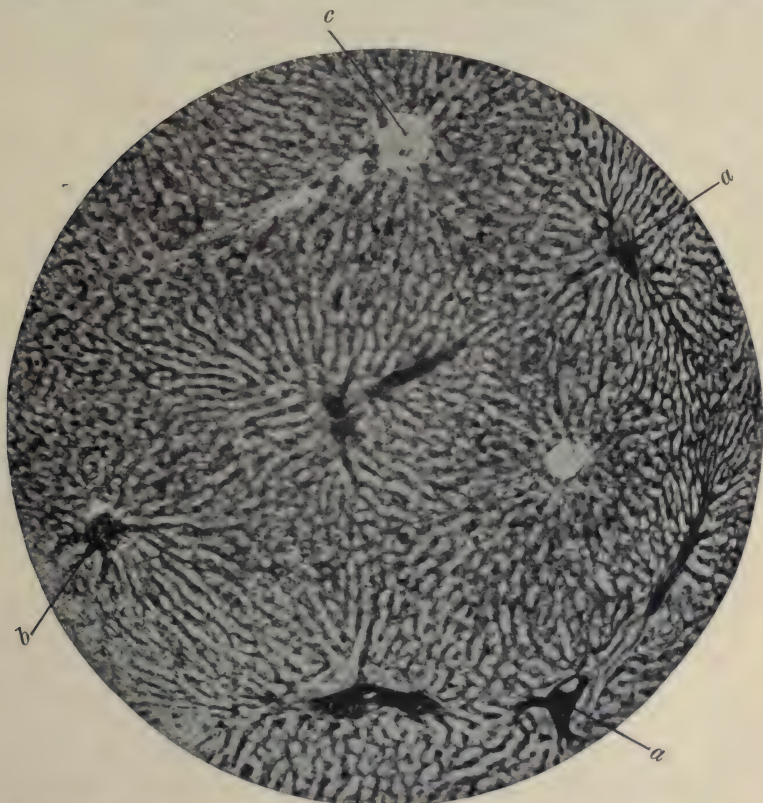


FIG. 274.—FROM A SECTION OF THE RABBIT'S LIVER WHOSE BLOOD VESSELS HAD BEEN INJECTED WITH A GELATINOUS, CARMIN STAINED, MASS; SOMEWHAT MORE THAN A SINGLE LOBULE IS REPRESENTED.

a, interlobular veins; *b*, central vein; *c*, central vein from which the injection mass had fallen out; the capillaries are dark. Photo. $\times 70$.

begins in the form of a Y, its two or more branches finally uniting to form a single vessel which pursues its course through the axis of the lobule. The central vein makes its exit at the periphery of the lobule and enters the interlobular connective tissue where it unites with its fellows to form larger *sublobular veins*. The sub-

lobular are easily distinguished from the interlobular veins by their thicker walls and by the fact that the former pursue an independent course through the tissue of Glisson's capsule, being nowhere in relation with either artery or duct.

The sublobular veins are, as a rule, vessels of considerable size, and by frequent union with their fellows become constantly larger. In their general direction they tend toward the dorsal surface of the liver and finally make their exit as four or five large *hepatic veins* which enter the inferior vena cava.

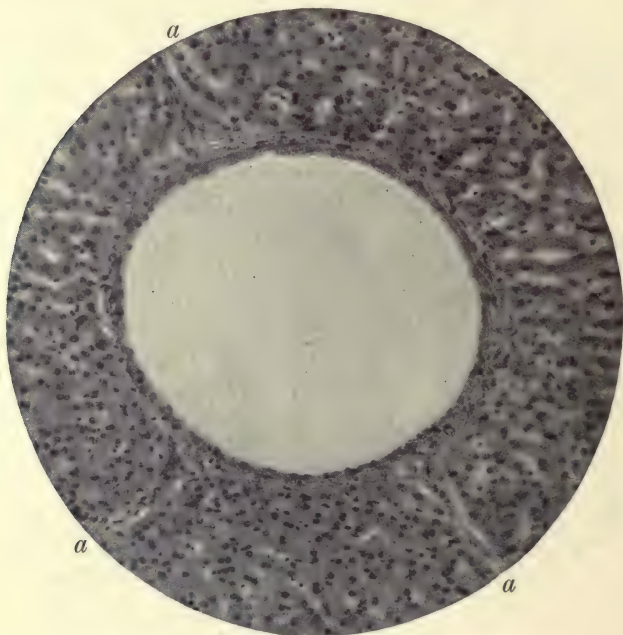


FIG. 275.—A SUBLOBULAR VEIN OF THE PIG'S LIVER.

a, capsule of Glisson between adjacent lobules. Hematein and eosin. Photo. $\times 60$.

The blood supply of the liver is peculiar in that: 1, the greater portion of its blood has already passed through the capillaries of the digestive organs before entering the liver; 2, its arterial supply is extremely insignificant, and supplies only the connective tissue framework, intermingling with the portal blood at the periphery of the lobule; 3, its intralobular capillaries are extremely abundant and are in intimate relation with the hepatic cells, each cell coming into contact with four to six capillary vessels.

The course of the blood through the vessels of the liver will be readily appreciated by reference to the following table which indicates the succession of the hepatic blood-vessels:

- | | |
|---------------------------------|---|
| 1. Portal vein. | 1. Hepatic artery. |
| 2. Interlobular veins. | 2. Interlobular arteries. |
| 3. Branches to lobule. | 3. Vaginal branches and capillaries in Glisson's capsule. |
| 4. Intralobular capillaries. | |
| 5. Central vein (intralobular). | |
| 6. Sublobular veins. | |
| 7. Hepatic veins. | |
| 8. Vena cava inferior. | |

The three classes of veins, interlobular, central, and sublobular are readily differentiated by the fact that the two latter lie alone, while the interlobular veins are always in company with ducts or arteries within the portal canals. Moreover the central vein has almost no connective tissue wall until near its exit from the lobule where it passes into the sublobular branches; the sublobular veins, on the other hand, possess a relatively thick connective tissue wall and even some smooth muscle, except in the very smallest, which are to be regarded as mere interlobular continuations of central veins which soon unite to form the larger sublobular vessels.

LYMPHATICS.—The lymphatics of the liver may be considered as consisting of a superficial set which supplies the hepatic peritoneum and the capsule of the liver, and which is continuous with a deeper set in Glisson's capsule. The lymphatics of the deep set begin as perivascular spaces within the lobule, from which the lymph enters larger lymphatic vessels in the interlobular connective tissue, which follow the vessels of the portal canals to their exit from the liver; the larger lymphatics pass to the abdominal lymphatic glands. Other lymphatics follow the sublobular and hepatic veins and pass to the mediastinal lymphatic glands.

NERVES.—The nerves of the liver are mostly of the non-medullated variety. They follow the portal canals and are distributed to the walls of the blood vessels, the walls of the bile ducts, and to the capsule of the

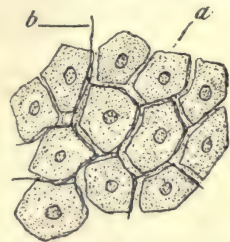


FIG. 276.—INTRALOBULAR NERVE FIBRES IN A RABBIT'S LIVER.

a, hepatic cells; *b*, nerve fibre. Golgi stain. Highly magnified. (After Berkley.)

liver. Naked fibrils from these trunks also enter the lobules and form a plexus among the hepatic cells (Korolkow*) in relation with which they form fine terminal brushes and varicose end knobs (Berkley†).

THE GALL BLADDER

The wall of the gall bladder consists of three coats: 1, mucous; 2, muscular; 3, fibro-serous. The mucous membrane is markedly folded or corrugated, the irregularly polygonal depressions being relatively broad at the fundus but becoming narrower toward the neck of the organ. The lining epithelium is of the tall columnar variety, with spheroidal or ovoid nuclei which lie near the base of

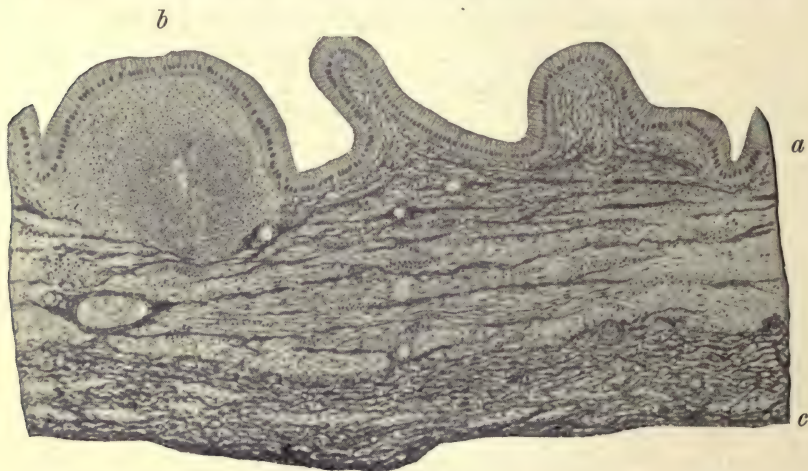


FIG. 277.—FROM A SECTION THROUGH THE WALL OF A DOG'S GALL BLADDER.
a, epithelium; b, lymphatic nodule; c, serous coat. $\times 80$. (After Sudler.)

the cell. The free extremity of the epithelial cells presents an indistinct cuticular border. The epithelium follows all the folds of the mucosa and lines the intervening depressions.

The corium of the mucosa consists of delicate connective tissue and contains a few smooth muscle fibres derived from the muscular coat. It is connected with the muscularis by a thin layer of denser connective tissue which contains blood and lymphatic vessels and which simulates a submucosa.

The gall bladder possesses a distinct muscular wall, consisting of numerous interlacing smooth muscle bundles the most of which

* Anat. Anz., 1893.

† Johns Hop. Hosp. Rep., 1895.

are circularly disposed. Occasionally they form fairly distinct circular and longitudinal layers.

The fibro-serous coat consists of loose areolar tissue, which contains the larger blood vessels with which the organ is abundantly supplied. The free surface of the gall bladder also receives a peritoneal investment.

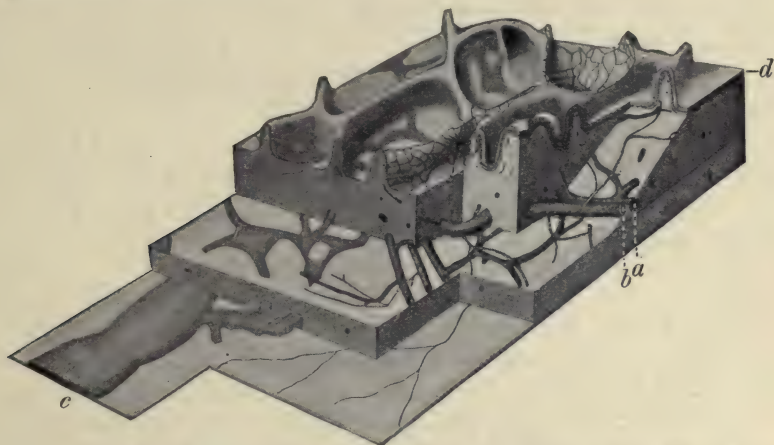


FIG. 278.—RECONSTRUCTION OF THE WALL OF A DOG'S GALL BLADDER.
a, vein; b, artery; c, lymphatic vessel; d, epithelium. $\times 60$. (After Sudler.)

Occasional mucous glands occur in the mucosa of the gall bladder. These are mostly of small size and widely separated, but toward the neck of the organ they increase in both number and size. They form short, branched, convoluted tubules.

The blood vessels form a plexus just outside the muscular coat, from which branches are distributed to the peritoneal coat and to a plexus in the depth of the mucosa from which capillaries are supplied to the muscular layers and to a subepithelial plexus. The nerves are distributed to the blood vessels and to the muscular wall. Minute ganglia occur in the muscular coat.

CHAPTER XIX

THE URINARY SYSTEM

THIS system includes the *kidneys*, which are two large secreting glands, together with their excretory passages, the *ureters*, which conduct the urine to the *urinary bladder*, whence it is voided through the *urethra*.

THE KIDNEY

Each kidney is a large secreting gland of the compound tubular type. Its secretion, the urine, is produced by the *uriniferous tubules*, which are long tortuous canals beginning near the surface of the kidney and finally ending at the hilum of the organ where they pour their secretion into the calyces of the renal pelvis. The uriniferous tubules are in intimate relation with the renal blood-vessels which supply rich capillary plexuses to the entire extent of the tubules. Each uriniferous tubule consists of both tortuous and straight portions, and these are so regularly disposed as to produce macroscopical variations in the appearance of the different portions of the renal parenchyma according as the tortuous or the straight portions of the tubules predominate. These variations result in the following topographical subdivisions.

TOPOGRAPHY OF THE KIDNEY (Figs. 288 and 290).—If the kidney be divided parallel to its long axis by an incision extending from its convex surface to the hilum, the cut surface shows that the parenchyma is divisible into a superficial cortex and a central medulla. The hilum of the organ forms a deep excavation which is occupied by the *renal pelvis* and its subdivisions, the *infundibula* and *calyces*, into which the medulla projects in the form of several conical pyramids. The pelvis of the kidney, the expanded funnellform beginning of the ureter, toward the renal parenchyma divides into two or three infundibula, which in turn subdivide into several calyces, each of which incloses the conical apex of a projecting medullary or *Malpighian pyramid*.

The Medulla of the kidney consists of a number of these conical Malpighian pyramids (usually twelve to fifteen) each of whose apices, as already stated, is received into the extremity of a renal calyx. The base of each Malpighian pyramid is embedded in the adjacent renal cortex, and that portion of the cortex which is interposed between the bases of adjacent pyramids, and thus brought into relation with the fibrous and adipose tissue which envelopes the pelvis and calyces at the hilum of the organ, composes the cortical *columns of Bertini*.

Each Malpighian pyramid may be subdivided into a central free portion, the apical or *papillary zone* of the medulla, which is received into a calyx, and an outer or basal portion, which is embedded in the renal cortex and is known as the *boundary zone* of the medulla. These two portions of the medulla, the papillary and boundary zones, can be readily distinguished, since the latter contains only narrow tubules and is highly vascular, while the former, relatively deficient in blood vessels, contains the broad terminations of the uriniferous tubules, the so-called *ducts of Bellini*, which converge toward the apex of the Malpighian pyramid where they open into the calyces.

The Cortex of the kidney, on careful observation, presents numerous dark lines or delicate columns which radiate from the base of the Malpighian pyramids outward toward the surface of the organ. These radiating columns are the *medullary rays** (*pyramids of Ferrein*). They contain straight portions of the uriniferous tubules, only these are continuous with the similar tubules in the boundary zone of the medulla.

That portion of the cortex which invests the medullary rays, and which includes all the remaining cortical portions of the organ, consists of extremely tortuous tubules, and is characterized by the presence of small globular bodies, each of which contains a tuft of capillary vessels. These are the *Malpighian bodies* (renal corpuscles) which are characteristic of the kidney. The portion of the cortex in which they occur includes the entire cortical substance with the exception of the medullary rays, and is known as the renal *labyrinth*. The labyrinth is subdivided into: 1, the *columns of Bertini*, already mentioned; 2, the intercolumnar

* These columns lie within the cortex and not, as their name might be taken to indicate, in the medulla. They are termed medullary rays because of their peculiar relation to the medulla, from which they extend outward in a radial direction.

portions, or *labyrinth* proper, which include that portion of the labyrinth which invests the medullary rays, and which, in sections cut parallel to these columns (longitudinal sections) appears as a portion of cortex inserted between the adjacent medullary rays; 3, a narrow *boundary zone* of the cortex, "*cortex corticis*" of Hyrtl, which is included between the fibrous capsule of the organ and

the tips of the medullary rays, and in which the Malpighian bodies, though present, are relatively few in number.

The Renal Lobule.—

In fetal and infantile life the kidney is distinctly lobulated. This condition is permanent in some animals, each lobe consisting of a Malpighian pyramid with its related portion of cortical substance. In man, after the first year, the renal lobes completely fuse and eventually leave scarcely a trace of the early lobar condition.

The term renal lobule or *reniculus*, as applied to the adult human kidney, refers to a still smaller subdivision of the organ, one which includes a single medullary ray together with that portion of the cortical labyrinth by which it is immediately invested. This lobule is the anatomical unit of the kidney and is

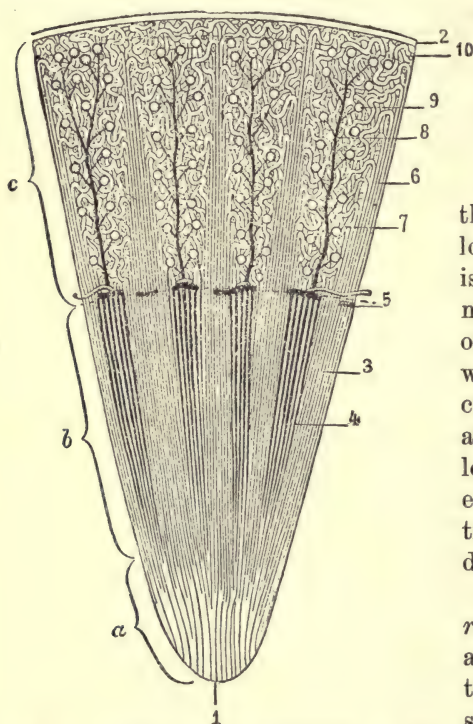


FIG. 279.—DIAGRAM OF THE STRUCTURE OF THE KIDNEY.

a, papillary zone, and *b*, boundary zone of the medulla; *c*, cortex; 1, apex of a Malpighian pyramid; 2, capsule; 3, tubules of the medulla; 4, vasa rectae; 5, vascular arcades; 6, a medullary ray; 7, labyrinth; 8, interlobular artery; 9, Malpighian body; 10, "*cortex corticis*." (After Testut.)

thus comparable to the hepatic or pulmonary lobule. The tortuous secreting portions of its uriniferous tubules are contained in the labyrinth at the periphery of the lobule, while its straight conducting portions lie in the medullary ray in the axis of the

lobule. The larger interlobular arteries and veins lie at the periphery, where they supply branches to several adjacent lobules.

THE RENAL CONNECTIVE TISSUES.—The kidney is enveloped by a fibrous *capsule* which is loosely attached to the substance of the organ and contains the usual proportion of elastic fibres together with a little smooth muscle. At the hilum of the organ the capsule is continuous with the connective tissue which envelops the renal pelvis, infundibula, and calyces, and which, in the intervals between adjacent calyces, comes into relation with the cortical substance of the columns of Bertini.

This connective tissue of the hilum is of the areolar variety and contains much adipose tissue. It supports the large arteries and veins as they pass along the surface of the renal pelvis on their way to and from the columns of Bertini, where they enter or leave the renal tissue. Sympathetic nerve fibres and a few small ganglia are also found in this region.

The connective tissue of the interior of the organ, *interstitial tissue*, is very scanty, and in most parts consists only of isolated fibrils which invest the blood vessels and the renal tubules. It forms a very delicate reticulum by which the walls of the uriniferous tubules are loosely united. If the epithelium of these tubules is removed, a delicate fibrous network remains; this network incloses a homogeneous basement membrane upon which the lining epithelium ordinarily rests. Elastic fibres scarcely occur among the tubules of the kidney. The interstitial tissue is slightly increased in amount about the larger blood vessels, the Malpighian bodies of the cortex, and the small blood vessels of the boundary zone of the medulla. At the apex of the Malpighian pyramid it invests the large ducts of Bellini in considerable quantity.

THE URINIFEROUS TUBULES.—The uriniferous tubules begin in the cortical labyrinth as the capsules of the Malpighian bodies. Assuming a tubular form they then pursue a tortuous course through the labyrinth and finally enter the boundary zone of the medulla, where, much reduced in size, they form the loop of Henle, which consists of a short, descending, thin limb, a U-shaped loop, and a long, ascending or thick limb. This last division, after recrossing the boundary zone of the medulla, enters a medullary ray and returns to the region of its origin, where it becomes again convoluted. A short arched tubule connects this convoluted portion with a straight collecting tubule of the medullary ray. The collecting tubules traverse the whole length of the medullary ray

uniting with their fellows and receiving other arched tubules along their entire course. They then cross the boundary zone of the medulla, and finally, in the papillary zone, form the large terminal tubules, ducts of Bellini, which pour the urinary secretion into the renal calyces.

Each uriniferous tubule may thus be subdivided into several portions which differ from each other, not only in their location, but also in the character of their lining epithelium. The successive portions which compose a single uriniferous tubule may be enumerated as follows:

1. Capsule of the Malpighian body.
2. Neck of the tubule.
3. Proximal convoluted portion.
4. Descending limb of Henle's loop.
5. Loop of Henle.
6. Ascending limb of Henle's loop.
7. Distal convoluted portion.
8. Arched collecting tubule.
9. Straight collecting tubule.
10. Duct of Bellini.

It should be borne in mind that all of these several portions form only successive parts of a single uriniferous tubule. Those portions of the urine which are secreted into the capsule of the Malpighian body must therefore find their

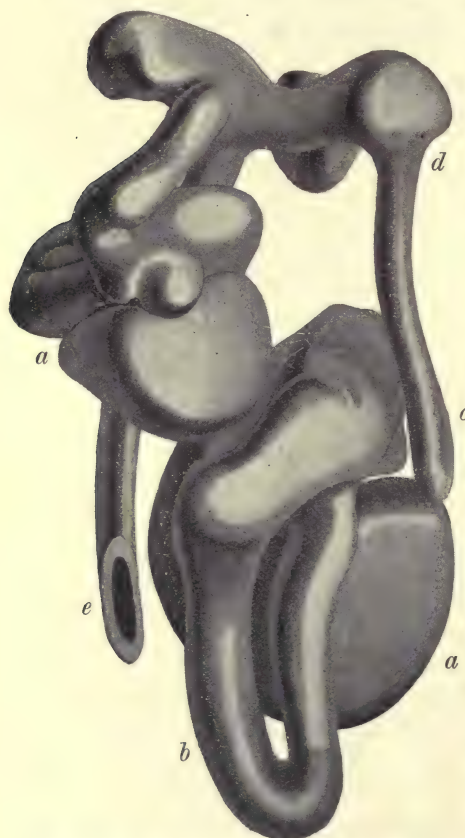


FIG. 280.—RECONSTRUCTION OF A URINIFEROUS TUBULE OF AN INFANT.

a, glomeruli; *b*, Henle's tubules; *c*, distal convoluted; *d*, junctional; *e*, collecting tubule. (After Stoerk.)

way through each of these successive portions before it can reach the excretory passages of the renal calyces, pelvis, and ureter.

1. **The Malpighian Body.**—A Malpighian body consists of a spherical tuft of capillary vessels, the *glomerulus*, which in the course of its development is invaginated into the end of the uriniferous tubule, and thus comes to be enveloped by a double layer of flattened epithelial cells known as the *capsule of Bowman*.

The one layer of Bowman's capsule, the quasi-visceral, closely invests the entire surface of the glomerulus except at that point where the afferent and efferent vessels enter and leave the capillary tuft; at this point the visceral epithelium is reflected outward and becomes continuous with the quasi-parietal layer. The surfaces of these two layers



FIG. 281.—RECONSTRUCTION OF A GLOMERULUS OF THE HUMAN KIDNEY.

a, afferent vessel; *b*, efferent vessel; *c*, capillaries. $\times 444$. (After Johnston.)

are almost in apposition; the narrow interval between them which results from the slightly eccentric position of the glomerulus forms the first portion of the lumen of the uriniferous tubule. At that pole of the Malpighian body which is opposite the entrance of its blood vessels the capsule opens, through a narrow neck, into the first or proximal convoluted portion of the uriniferous tubule.

The glomerulus is a true arterial *rete mirabile*,* since it receives an afferent artery, which, after forming the capillaries of the glomerulus, passes out as an efferent artery to again enter a capillary plexus about the neighboring tubules of the renal cortex. The afferent vessel is of somewhat larger caliber than the efferent, a noteworthy fact because of its relation to the intraglomerular blood pressure.

On entering the glomerulus the artery divides into two vessels which immediately subdivide with the formation of five branches

* *Retia mirabilia* are formed by the rapid division of a blood vessel, the resulting capillaries being as promptly reunited to form an efferent vessel of the same character as the afferent. *Retia mirabilia* may be either arterial or venous.

(Johnston*). Each of these branches forms a series of anastomosing capillary loops whose convexity is directed away from the entering artery. The capillary loops reunite, in a similar manner,

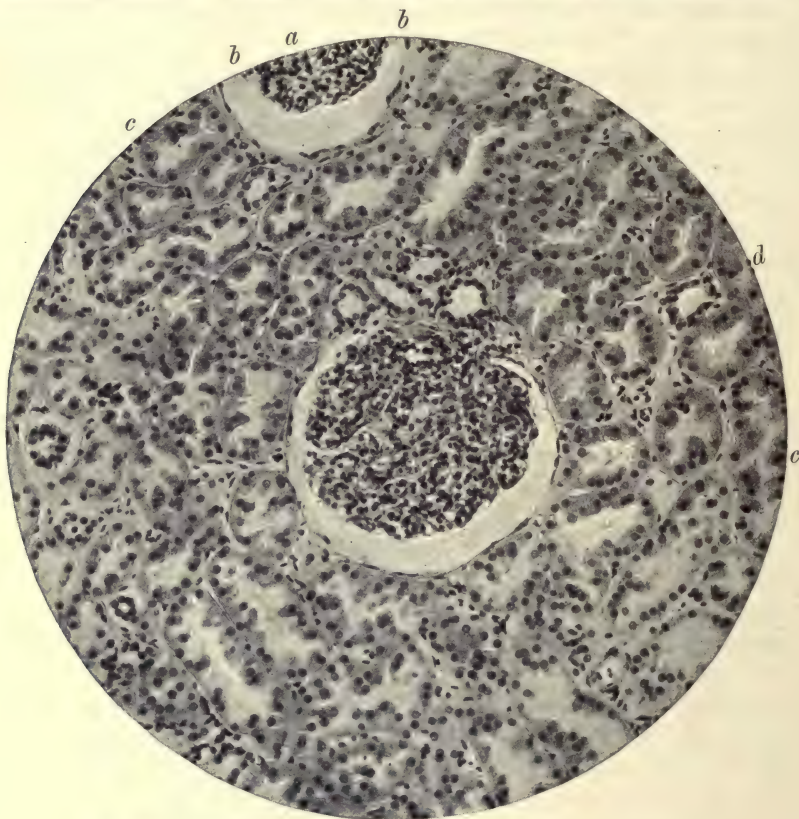


FIG. 282.—FROM THE CORTICAL LABYRINTH OF THE HUMAN KIDNEY.

A large Malpighian body is in the center of the figure. At its upper border are several sections of distal convoluted tubules. The great majority of the tubules shown are from the proximal convoluted portions. *a*, a portion of a glomerulus; *b-b*, parietal layer of Bowman's capsule; *c*, proximal convoluted tubules; *d*, just within this point is a transection of a junctional tubule having relatively low and clear epithelium and a broad lumen. Hematein and eosin. Photo. $\times 135$.

to form the efferent vessel, which leaves the glomerulus in company with the afferent; but, once out, they soon part company, the efferent vessel breaking into a second capillary plexus about the neighboring tubules. Within the glomerulus the capillaries are

* Johns Hop. Hosp. Bull., 1900.

united by a very delicate but scanty connective tissue containing no elastic fibres.

The visceral layer of Bowman's capsule is firmly adherent to the walls of the glomerular capillaries. It consists of a single layer of flat epithelial cells which are intimately blended with each other and with the endothelium of the capillaries. The epithelial cells possess a clear cytoplasm and a flattened ovoid nucleus, which, being thicker than the body of the cell, produces a considerable bulging. In fetal and infantile life the shape of the cells of this layer is cuboidal or even low columnar, but becomes more and more flattened as development progresses, until the epithelium finally simulates a layer of endothelial cells.

The epithelium of the parietal layer of Bowman's capsule is also cuboidal in fetal life, but during development becomes nearly as much flattened as that of the visceral layer. Its single layer of finely granular cells forms a complete lining for the capsule. It rests upon a homogeneous basement membrane which is invested by a thin layer of connective tissue. This fibrous layer is rather more highly developed about those Malpighian bodies which lie near the medulla than about those of the more peripheral portions of the cortex.

2. The Neck of the Tubule.—In this portion of the tubule the flattened epithelium of Bowman's capsule rapidly changes to the low columnar type of the proximal convoluted portion. This section is extremely short; it forms a constricted portion which marks the beginning of the tortuous tubule. This constriction is more apparent than real, since the caliber of the tubule in the neck is as great as in the succeeding portion whose external diameter is, however, much increased by the increasing height of the epithelial cells. This portion of the tubule, being in relation with the Malpighian body, is necessarily found in the cortical labyrinth.

3. The Proximal Convoluted Portion (*Tubulus Contortus, First Convoluted Tubule, Convoluted Tubule of the First Order*).—This is the longest and broadest portion of the uriniferous tubule. Collectively the convoluted tubules form the greater part of the cortical labyrinth, in which region only they occur. This portion of the tubule is remarkable for the irregularity of its course, it being twisted and bent upon itself in a most tortuous manner. Arising at the Malpighian body, it at first passes toward the surface of the organ (Golgi*), but soon turns about and runs toward the medulla,

*Rend. d. r. accad. d. Lincei, 1889.

at first with extreme convolutions, but later pursuing a rather spiral course (*spiral tubule* of Schachowa). On reaching the border of the medulla the tubule becomes sharply constricted and enters the medullary boundary zone at the thin descending limb of Henle's loop.

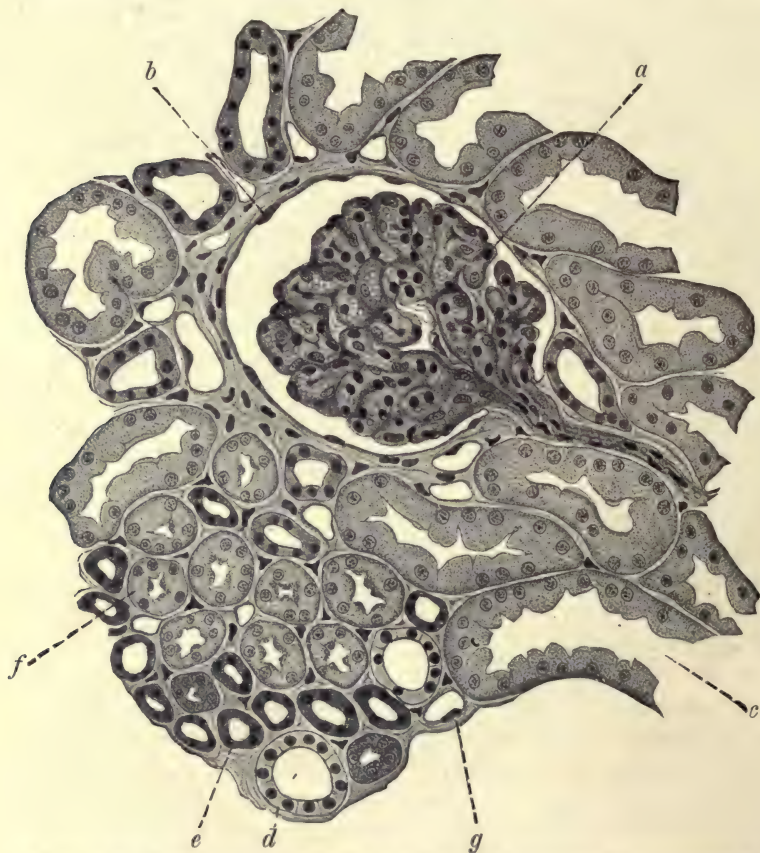


FIG. 283.—FROM THE CORTX OF THE HUMAN KIDNEY, SHOWING A TRANSECTION OF A MEDULLARY RAY IN THE LOWER LEFT-HAND CORNER.

a, glomerulus; *b*, capsule of Bowman; *c*, proximal convoluted tubule; *d*, collecting tubule; *e*, ascending limb of Henle's tubule; *f*, spiral tubule; *g*, blood vessel. Hematoxylin. $\times 200$. (After Schaper, from Stöhr.)

The epithelium of the convoluted tubule is of the columnar or pyramidal type, its cells having broad, firmly united bases and conical free apices. The lateral margins of the cells are often so intimately blended at the base as to resemble a syncytium. When

isolated, or if outlined by impregnation with silver salts, the borders of the epithelial cells are extremely irregular and are deeply fluted or serrated, the serrations of each cell interdigitating with those of its neighbors. The deep fluted serrations of the interlocked epithelium gives many of its cells a coarsely striated appearance, the striation being more prominent beneath the centrally situated nucleus than in the apical portion of the cell. Other longitudinal striations in the proximal or basal portion of the cell are the result of a linear arrangement of the coarse granules which occur in this part (R. Heidenhain*). These appearances often give the epithelium of the convoluted tubules a peculiar striated or "rodged" character.

The apices of the epithelial cells are very easily destroyed, but when perfectly preserved often present a delicately striated, cuticular border. The remaining portions of the cytoplasm are finely granular.

The nuclei of the epithelial cells of the convoluted tubules are spherical in shape, and do not stain very deeply with nuclear dyes as compared with the more distinct and deeply staining nuclei of the collecting tubules. Thus they appear as if partially clouded by the granular cytoplasm, an appearance which is greatly exaggerated with the onset of acute inflammatory processes, which, on attacking the kidney, are prone to involve the convoluted tubules. The chromatin is quite evenly distributed throughout the nucleus and the nuclear membrane is not easily demonstrated.

The lumen of the convoluted portion of the uriniferous tubule is of variable caliber; it presents frequent slight dilatations.



FIG. 284.—FROM A LONGITUDINAL SECTION OF A CONVOLUTED TUBULE OF THE GUINEA PIG'S KIDNEY.

The cell outlines have been blackened by the Golgi method. Very highly magnified. (After Landauer.)

* Arch. f. mik. Anat., 1874.

The caliber also depends, to some extent, upon the secretory activity of the epithelium, whose cells become shrunken, and the lumen correspondingly dilated, during active secretion. The convoluted tubules are most actively engaged in the secretion of urine, but the further changes accompanying their secretion have not yet been satisfactorily demonstrated.

4. Descending Limb of Henle's Tubule (*the Thin or Narrow Tubule of Henle*).—In this portion, which is, typically, located in the boundary zone of the medulla, the uriniferous tubule becomes very much narrowed, but the decreased diameter is the result of diminished height of the lining epithelium rather than of any change in the caliber of the tubule. The length of this portion of the tubule is very variable; typically it corresponds very nearly with the breadth of the medullary boundary zone.

The lining epithelium of the descending limb is of a peculiar flattened shape. Its cells possess an ovoid nucleus which, being thicker than the surrounding portions of the cell, projects slightly into the lumen of the tubule. The bulging nuclei of opposite sides of the tubule are not in apposition but interlock with one another, the nuclei of one side of the tubule being opposed to the cell margins of the opposite side. The lumen of longitudinal sections through the axis of the tubule thus acquires a sort of zigzag outline. The nuclei stain deeply but possess an evenly distributed chromatin. The cytoplasm of the epithelium is very finely granular, and although its cells are intimately adherent at their lateral margins they do not present the typical striations which are characteristic of the preceding portion.

5. The Loop of Henle.—As the descending limb enters the loop of Henle the tubule makes an abrupt turn and returns toward the cortex. The location of the loop, being dependent upon the uncertain length of its descending and ascending limbs, is very variable. It may be found in any portion of the medulla except the extreme tip of the Malpighian pyramids; its most frequent site, however, is near the junction of the boundary and papillary zones.

The structure of the loop may be that of either the descending or the ascending limb. It is also subject to great variations, since the change in structure from the narrow to the broad type, though it typically occurs just prior to the formation of the loop, is frequently delayed until well into the ascending limb. As a rule the change in type occurs earlier when the loop lies in the boundary zone, and later when it occurs nearer the apex of the Malpighian

pyramid; the thick ascending limbs do not occur in the papillary zone of the medulla.

6. **The Ascending Limb of Henle's Loop** (*the Broad or Thick Limb*).—This portion of the tubule returns through the boundary zone of the medulla and enters a medullary ray, its course being parallel to that of the descending limb. It then travels toward the

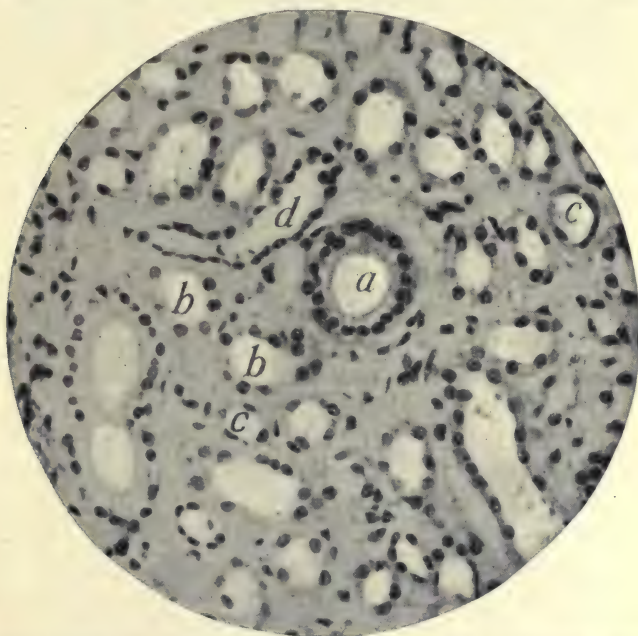


FIG. 285.—A GROUP OF TUBULES FROM A TRANSECTION OF A MALPIGHIAN PYRAMID OF THE HUMAN KIDNEY; THE SECTION PASSES THROUGH THE BOUNDARY ZONE.

a, collecting tubule; *b*, ascending limb of Henle's loop; *c*, descending limb; *d*, loop of Henle. Hematein and eosin. Photo. $\times 275$.

surface of the kidney, but finally leaves the ray and enters the labyrinth to reach that Malpighian body from which the uriniferous tubule took origin (Golgi) and in relation to which the tubule again acquires a tortuous course (distal convoluted portion). Within the boundary zone of the medulla this portion of the tubule is much broader than the preceding division, but it becomes somewhat reduced in size in its course through the medullary ray.

The epithelium of the ascending limb is of a short cuboidal form. Its cytoplasm resembles that of the lining epithelium of the convoluted portion, although the nuclei in the tubule of Henle

are rather more distinct. Basal striations are also less distinct than in the convoluted tubule, the lateral serrations less deep, and the cell outlines sharper. The cells of this portion frequently possess a slightly imbricated arrangement.

7. The Distal Convoluted Portion (*Intercalary or Intermediate Portion, Convoluted Tubule of the Second Order*).—This portion of the uriniferous tubule begins close to the vascular pole of the Malpighian body, and, after several irregular contortions which are confined to the region of the cortical labyrinth, enters an arched collecting tubule. The distal is much shorter than the proximal convoluted portion. Its caliber is subject to great irregularities, so much so that its early turns have been characterized as the irregular or zigzag portion of the uriniferous tubule. The epithelium of this section resembles that of the proximal convoluted portion but is lower, more cuboidal, and striations are indistinct.

This portion terminates the typically secretory portion of the uriniferous tubule. Beyond here the tubule possesses more the function of a duct, hence its epithelium shows a decided change in character. Hitherto it has possessed the peculiar character, the typically granular cytoplasm, of a secreting type of cell. Beyond this section the epithelium is no longer so granular but possesses a characteristically clear appearance.

8. The Arched Collecting Tubule (*Curved or Junctional Tubule*).—This is a short portion of the uriniferous tubule which connects the distal convoluted portion in the cortical labyrinth with the straight collecting tubules of the medullary rays. Its course is characteristically arched.

The epithelium of the arched tubule consists of clear cuboidal cells with distinct outlines and deeply stained, sharply defined nuclei. The chromatin of the nucleus is irregularly distributed, forming numerous karyosomes, and the nuclear membrane is distinct. The cytoplasm is relatively devoid of granules, and unlike that of the secreting epithelium does not possess a strong affinity for the acid dyes (eosin, etc.).

9. The Straight Collecting Tubules.—These portions of the tubules begin in the medullary rays, where they receive the arched tubules, and, proceeding to the medulla, become considerably increased in size. They penetrate the boundary zone of the medulla, all pursuing a parallel or slightly convergent course, and occasionally uniting with each other. On entering the papillary zone, by

frequent union they become rapidly larger, and in the apex of each Malpighian pyramid finally form about a score of large terminal tubules, the ducts of Bellini. Though shorter than the convoluted

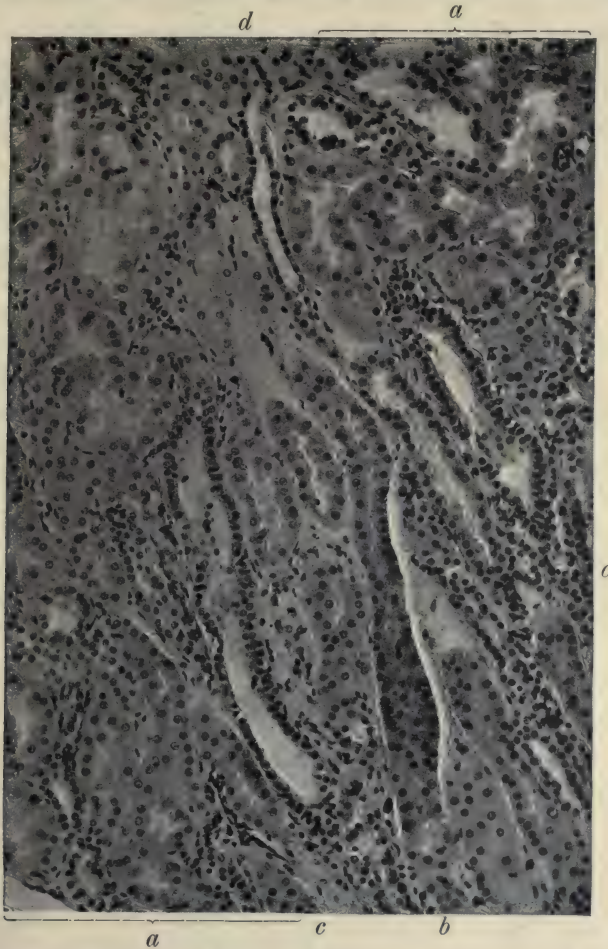


FIG. 286.—FROM THE CORTEX OF THE HUMAN KIDNEY; A MEDULLARY RAY IN OBLIQUE SECTION.

a, labyrinth; *b*, spiral tubule; *c*, *c*, collecting tubules; *d*, Henle's tubule. Hematein and eosin. Photo. $\times 135$.

tubules, the straight collecting portions, because of their direct course, traverse a broader area of the renal tissue; beginning near the peripheral end of the medullary rays, in these columns they

cross nearly the whole breadth of the renal cortex and entering the medulla extend from base to apex of the Malpighian pyramid.

Throughout their whole course they progressively increase in size and caliber. A corresponding progressive increase in the height of their epithelial cells likewise occurs, so that the lumen of the straight tubules of the medulla is not only actually greater than that of those of the medullary rays, but the walls of the former tubules are also considerably thicker. The extreme of this progression is found in the broad lumen and tall epithelium of the ducts of Bellini.

The epithelium of the straight tubules, like that of the arched, possesses a clear cytoplasm, distinct and deeply staining chromatic nuclei, and well defined cell outlines. Beginning in the medullary rays with a low columnar type, it gradually increases in height in the course of the tubule until, in the papillary zone, the epi-

thelium acquires a tall columnar form. The clear cytoplasm and distinct nuclear membranes of the epithelium of the collecting tubules stand out in sharp contrast to the granular cytoplasm and the evenly distributed chromatin in the nuclei of the lining cells in the secreting portions of the uriniferous tubules.

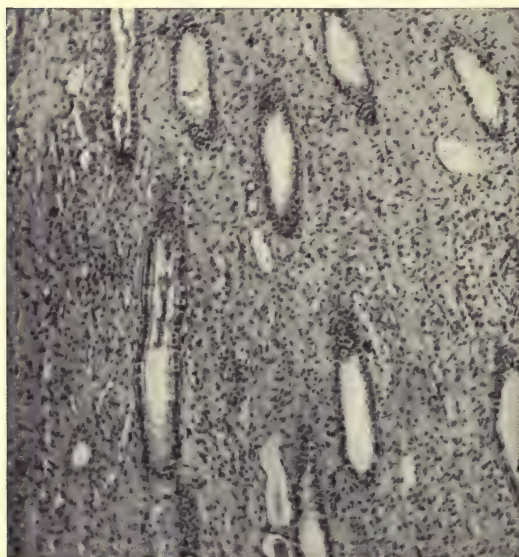


FIG. 287.—DUCTS OF BELLINI IN OBLIQUE AND LONGITUDINAL SECTION, NEAR THE APEX OF A MALPIGHIAN PYRAMID IN THE HUMAN KIDNEY; FROM THE PAPILLARY ZONE OF THE MEDULLA.

Hematein and eosin. Photo. $\times 450$.

10. The Ducts of Bellini (*Papillary Ducts*).—These are the wide mouths of the uriniferous tubules which are formed by the dicot-

omous union of the collecting tubules and which empty their secretion into the renal calyces at the apex of the Malpighian pyra-

mids. They are lined by tall columnar cells with an exceptionally clear cytoplasm which has an affinity for the basic in preference to the acid class of dyes. The nuclei are spheroidal or ovoid in shape and lie in the basal portion of the cell. At their termination several ducts of Bellini frequently open into a common depression or foveola which is lined by an involution of the layer of transitional epithelium, derived from that of the renal calyx, by which the free papillary portion of the Malpighian pyramid is clothed.

It is obvious that the entire uriniferous tubule, from the capsule of Bowman to the duct of Bellini, is a continuous tube whose epithelial wall, supported by a thin homogeneous basement membrane varies in character in each succeeding portion. Thus the proximal and distal convoluted portions and the ascending limbs of Henle's loops possess a granular, rodde or striated, acidophile, secreting epithelium; the capsule of Bowman has thin cells of an endothelial type; the descending limb and loop of Henle are lined by flattened finely granular and faintly acidophile epithelium; the curved and straight collecting tubules and ducts of Bellini possess a clear columnar epithelium. It should also be noticed that the several portions of the uriniferous tubule occur in different topographical subdivisions of the kidney and that, therefore, each of the subdivisions contains only certain characteristic portions of the uriniferous tubule. Thus are found in the—

	{	Malpighian body.
	{	Neck of the tubule.
CORTICAL LABYRINTH.	{	Proximal convoluted portion.
	{	Distal convoluted portion.
	{	Arched collecting portion.
	{	Spiral portion of the convoluted tubule.
MEDULLARY RAYS. . . .	{	Ascending limb of Henle's tubule.
	{	Straight collecting portion.
	{	Descending limb of Henle's tubule.
BOUNDARY ZONE OF	{	Ascending limb of Henle's tubule.
THE MEDULLA. . . .	{	Straight collecting portion.
	{	Descending limb of Henle's tubule.
PAPILLARY ZONE OF	{	Loop of Henle's tubule.
THE MEDULLA. . . .	{	Straight collecting portion.
	{	Duct of Bellini.

The following tabular *résumé* may be of service by emphasizing the more important peculiarities of the several portions of the uriferous tubule.

PORTION OF TUBULE.	EPITHELIUM.	LOCATION.
Malpighian body.	Flattened, endothelial.	Cortical labyrinth.
Neck.	Changing from flattened to low columnar.	Cortical labyrinth.
Proximal convoluted.	Low columnar, granular, and rodde.	Cortical labyrinth.
Spiral portion of above.	Low columnar, granular, and rodde.	Medullary rays of cortex.
Descending limb.	Low cuboidal or flattened, granular.	Medulla (boundary and papillary zones).
Loop.	Varies; like either the preceding or following.	Medulla (boundary and papillary zones).
Ascending limb.	Cuboidal or low columnar, granular, imbricated.	Boundary zone of medulla and medullary rays of cortex.
Distal convoluted.	Low columnar or pyramidal, granular, and rodde.	Cortical labyrinth.
Arched collecting.	Cuboidal, clear cytoplasm, dark nucleus.	Cortical labyrinth.
Straight collecting.	Cuboidal, changing to columnar.	Medullary rays of cortex, and both zones of medulla.
Duct of Bellini.	Cuboidal, tall columnar.	Papillary zone of medulla.

BLOOD SUPPLY.—The kidney receives its blood supply from the renal artery, which, as it enters the hilum, divides into two sets of principal branches, of which the ventral set supply one-fourth, the dorsal set three-fourths of the renal substance. These principal branches, the *arteriæ propriæ renales*, are embedded in the connective tissue of the hilum and follow the walls of the infundibula and calyces, upon which they lie, thus reaching the columns of Bertini between the renal calyces. Here they enter the cortical substance and divide, each branch passing in a curved or arched manner beneath the base of the adjacent Malpighian pyramids. These vessels form an incomplete arterial arcade which lies in the margin of the cortex at the outer border of the medullary boundary zone.

From the arterial arcade, branches are given to the medullary tissue of the Malpighian pyramids on the one hand, and on the other to the cortical substance. Those branches which enter the medulla are slender vessels which pursue a characteristically straight course between the parallel tubules of this region and are

axis of the corpus spongiosum from its bulb forward to the urinary meatus at the tip of the glans penis. This canal has already been sufficiently described in the preceding chapter.

The skin of the glans penis is peculiar in the relatively moist character of its epidermis and the consequent imperfect development of its superficial horny layer. Its dermal papillæ are conspicuously developed. In the region of the corona the derma contains a ring of large sebaceous glands, the *glands of Tyson*, which open on the free epithelial surface. Their secretion forms the *smegma*, a peculiarly odoriferous sebum.



FIG. 299.—THE ERECTILE TISSUE OF THE PENIS.

c r, peripheral capillary plexus; *t a*, tunica albuginea; *v s*, venous spaces; *z*, bands of smooth muscle and vascular connective tissue. $\times 30$. (After Kölliker.)

The nerves of the penis are abundantly supplied with special nerve end organs. In the skin they form free varicose endings among the epithelial cells, and are connected with tactile corpuscles of Meissner in the dermal papillæ. Deeper in the skin are many end bulbs of Krause, while still deeper are the peculiar genital corpuscles. Pacinian corpuscles are also found in the loose connective tissue and in the tunica albuginea of the corpora cavernosa. Nerve fibres are abundantly supplied to the walls of the blood vessels.

The lymphatics of the penis form an abundant superficial set in the subcutaneous tissue; these follow the larger blood vessels and empty into the inguinal lymphatic glands. A less abundant deep set of lymphatics in the erectile tissue, also, accompanies the blood vessels of these parts, but are distributed to the pelvic lymphatic glands.

THE SEMEN AND SPERMATOOA

The essential constituent of the semen is the spermatozoön (*spermatozome*, *spermatozoid*), a body which is developed in the seminiferous tubules of the testes by the metamorphosis of the

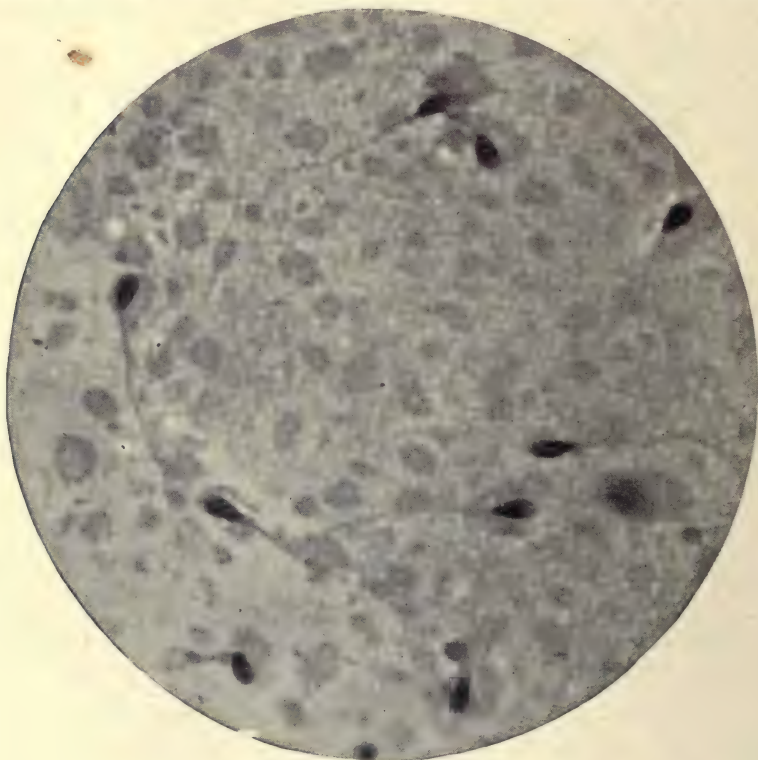


FIG. 300.—HUMAN SEMEN.

Hematein and eosin. Photo. $\times 850$.

cells of the lining epithelium. They are very numerous, a cubic millimeter of semen being said to contain as many as 60,876 spermatozoa (Lode*). In addition to the spermatozoa the semen

* Arch. f. Anat. u. Physiol., 1896.

contains the fluid secretions of the accessory genital glands and many coarse protoplasmic *seminal granules*. When first formed the spermatozoa are motionless, but when the secretion of the testes is diluted with the secretions of the seminal vesicles and prostate they become very active and retain their motility for a long time even under the most unfavorable conditions.

The spermatozoa are flagellate bodies which consist of a head, a middle piece, and a tail. Each of these subdivisions is a composite structure. The head of the human spermatozoön is an ovoid body about 4.5 to $5\ \mu$ long, 3 to $3.5\ \mu$ broad, and 0.5 to $1\ \mu$ thick. When seen "on the flat" (surface view) its outline is oval but when viewed in profile it has a pyriform shape. It is united to the middle piece by a slightly constricted neck and its anterior extremity forms a blunt point analogous to the "lance" of the spermatosomes of certain of the lower vertebrates. The head of the human spermatozoön consists of two distinct portions, a posterior solid mass of chromatin which stains deeply with nuclear dyes, and an anterior clear portion or head cap. This head cap in some of the mammalian species contains a rounded chromatic body, the acrosome.

At the posterior pole of the nuclear chromatin, where it joins the middle piece, is a small dark dot, the inner *centrosome*, from which the *axial filament*, beginning with a minute end knob, is continued backward through the middle and tail pieces and is inclosed by a delicate cytoplasmic envelope. At the tip of the tail piece the axial fibre is no longer surrounded by cytoplasm but projects as a naked *end piece*. The flagellum varies in diameter from a breadth of about $1\ \mu$ in the middle piece, to the immeasurably delicate end piece; in length it is about 45 to $50\ \mu$.

In the spermatozoa of the lower animals still other structures may be demonstrated in the flagellum, chief among which are (1)

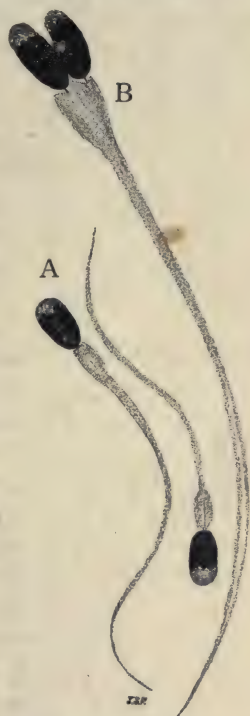


FIG. 301. — SPERMATOSOMES FROM THE SEMEN OF MAN.

A, usual type; B, "giant" double spermatozoön. Hematein and eosin. $\times 1200$.

the spiral cytoplasmic fin of the flattened spermatozoa of amphibians, whose border contains a second filament, the *marginal fibre*; (2) the faintly *chromatic ring* or spiral which sometimes occurs



FIG. 302.—SPERMATOOA OF VARIOUS ANIMALS.

A, from the badger;
B, from the bat. Redrawn after Ballowitz. $\times 1200$.
C, from the rat. Hematein and eosin. $\times 1200$.

near the posterior end of the middle piece or entwined about its axial filament. These structures have not, however, been demonstrated in the spermatozoa of man.

The spermatozoa may be regarded as metamorphosed germ cells which arise by the direct transformation of the spermatids in the seminiferous tubules of the testicle. As a result of this transformation, so far as has been satisfactorily demonstrated, the nucleus of the spermatid becomes the chromatic body or nucleus of the spermatozoön: the centrosome of the spermatid, usually double, enters the middle piece, the inner centrosome forming the end knob of the axial filament, the outer centrosome either forming the ring body of the middle piece or, like the inner, entering into the formation of the end knob and axial filament; the arcoplasm (attraction sphere, idiosome of Meves) leaves the centrosomes of the spermatid and in part at least wanders around the nucleus to the opposite pole where it forms the acrosome, the remainder of the arcoplasm probably entering into the formation of the cytoplasmic portion of the middle piece: the axial filament arises under the influence of the centrosomes (Meves*) or possibly by the direct transformation of the outer of these bodies (Korff,† Suzuki‡): and finally, the envelope of the

tail piece, and probably also that of the middle piece, arises by the direct transformation of a part of the cytoplasm of the spermatid; the remaining portion of the cytoplasm of the spermatid does not enter into the structure of the spermatozoön but is separately cast off and degenerates.

* Arch. f. mik. Anat., 1897.

† Ibid., 1899.

‡ Anat. Anz., 1898.

THE TESTIS (*Testicle*)

Each testis is inclosed within a serous sac, its *tunica vaginalis*, whose visceral layer is closely applied to the organ. Its parietal layer forms a lining membrane for the scrotum, within which the testicle is suspended. The tunica vaginalis is developed as an invagination of the peritoneum and is a true serous membrane. Its visceral endothelium rests upon a dense connective tissue layer, the *tunica albuginea*, which serves as a capsule for the organ. The deep surface of the membrane contains many blood vessels which are held in place by a somewhat looser type of connective tissue; hence this innermost coat is frequently termed the *tunica vasculosa testis*.

At the posterior border of the testis its connective tissue capsule presents a considerable thickening which indents the organ

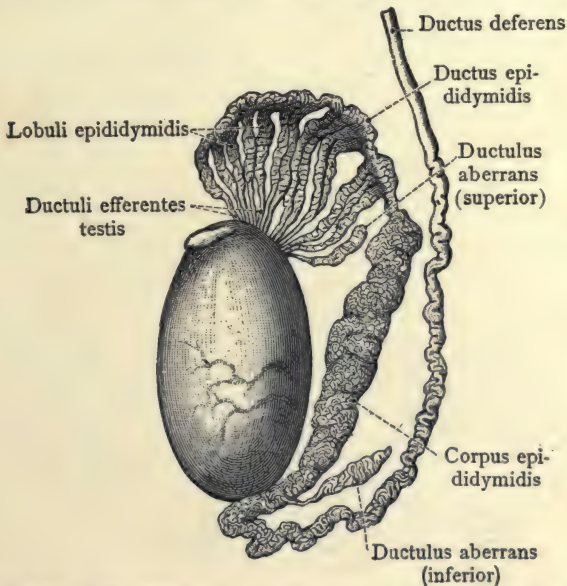


FIG. 303.—THE TESTICLE WITH ITS SYSTEM OF EFFERENT PASSAGES.

Natural size. (After Toldt.)

and extends well into its interior to form the *mediastinum testis* or body of Highmore, in which are the ducts of the *rete testis*. From the mediastinum testis fibrous septa radiate in all directions to become continuous at the surface of the organ with the connective tissue of the tunica albuginea. Thus the organ is sub-

divided into a number of pyramidal lobules whose bases rest upon the capsule and whose apices are directed toward the mediastinum. Each of these lobules contains numerous seminiferous tubules which are tortuous throughout the greater part of their course,

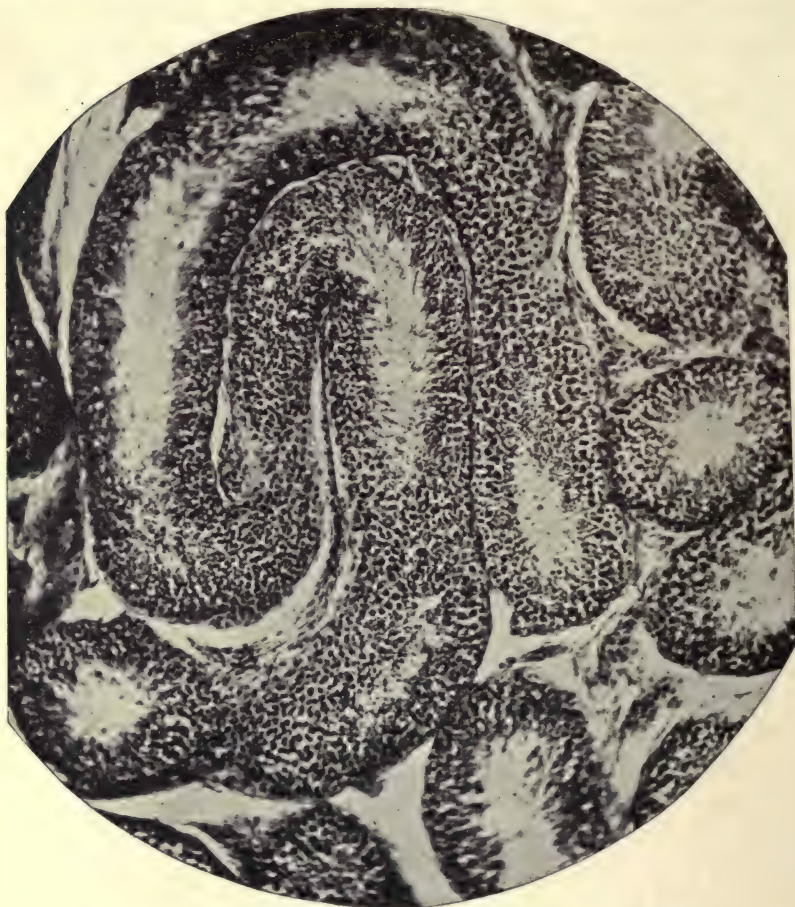


FIG. 304.—TORTUOUS SEMINIFEROUS TUBULES OF THE RABBIT'S TESTIS.

Hematein and eosin. Photo. $\times 214$.

but become straight, *tubuli recti*, toward the apex of the lobule, where they enter the mediastinum to become continuous with the canals of the rete testis.

The seminiferous tubules are invested with a delicate connective tissue which forms an intralobular framework. This

interstitial tissue is characterized by the presence of many peculiar ovoid *interstitial cells* of large size, whose significance is not yet determined. They contain a large nucleus which has a distinct nuclear membrane, a reticular chromatin network, and many karyosomes. Their cytoplasm is reticular and finely vacuolated.

The *seminiferous tubules* begin at the periphery of the organ with either a blind extremity or very frequently a peripheral loop formed by the anastomosis of adjacent tubes. They pursue their way through the lobule in an extremely tortuous manner (*tortuous* or *serpentine tubule*), and finally near the apex of the lobule become relatively straight (*tubuli recti*). They then enter the mediastinum and by frequent anastomoses form the rete testis. The tortuous portion of the seminiferous tubule is relatively long, its straight portion very short. It is the former which is of the greater physiological importance and which is to be considered as the true seminiferous tubule, for it is here that the spermatozoa, the essential elements of the semen, are produced. The straight tubules mark the beginning of a system of excretory ducts which include the ductuli efferentes, epididymis, vas deferens, ejaculatory duct, and urethra.

The tortuous seminiferous tubules are lined by a peculiar form of epithelium, which, since it consists of several layers of spheroidal cells, might be described as a stratified spheroidal type. The tubule is invested by a very delicate tunica propria upon whose homogeneous basement membrane the epithelium rests.

The cells of the lining epithelium are divisible into three types, which are from without inward: 1, a single layer of small cuboidal *spermatogonia*; 2, one or two rows of very large *spermatocytes*; 3, and three to five rows of spheroidal *spermatids*. Besides these a *fourth* type of cell occurs at fairly regular intervals in the circumference of the tubule; these are the so-called *Sertoli's cells*. These last cells are of columnar form, rest upon the membrana propria and extend inward for a variable distance, sometimes penetrating as far as the innermost cell layers. The developing spermatozoa are, at a certain stage, intimately united with the central ends of the Sertoli cells, the resulting group—a supporting cell of Sertoli with its attached spermatozoa—forming the so-called *spermatoblasts** of von Ebner †.

* Much confusion has arisen through the use of this term by certain authors as synonymous with the term spermatid.

† Untersuch. a. d. Inst. f. Physiol. u. Hist., Graz, 1871.

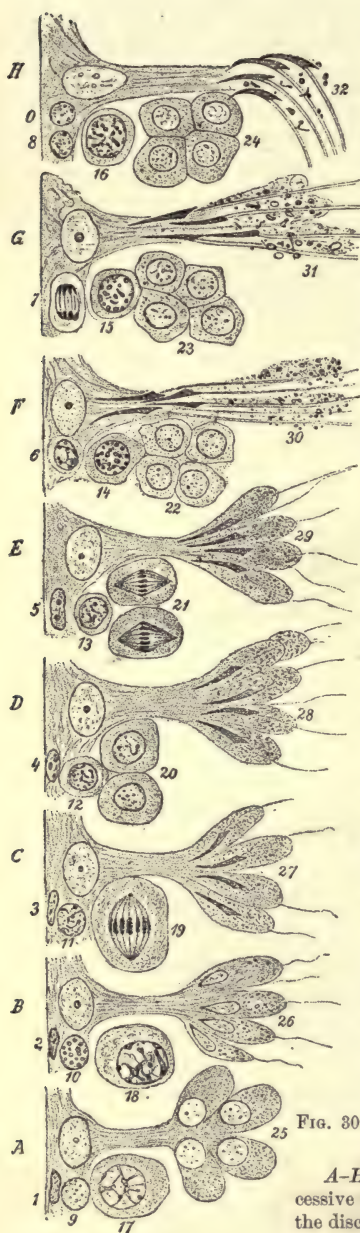


FIG. 305.—DIAGRAM OF THE SUCCESSIVE STAGES OF SPERMATOGENESIS IN THE RAT.

A-H, the grouping of associated stages; 0-32, the successive steps, in numerical order, from the spermatogonia to the discharge of the spermatozoa. (After Kölliker.)

The four types of epithelial cells enumerated above may also be considered as typifying the four principal stages in the origin and development of the spermatozoa. Spermatogenesis begins with the spermatogonia which, by reproduction, differentiation, and development, pass successively through the spermatocyte, spermatid, and spermatoblast stages to finally produce the mature spermatozoa. In the course of this development great changes are produced in the character of the lining epithelium, each of the several cell types presenting many intermediate phases (Fig. 305). Hence, in a given lobule of the testis, tubules may be found which present over and over again all of the successive phases of spermatogenesis, and scarcely any two neighboring tubules, nor the successive portions of a given tubule, will at the same time present the same phases of spermatogenesis. It is estimated that in every 32 mm. of the length of a tortuous tubule the several phases of spermatogenesis are repeated (von Ebner*).

The **spermatogonia** are small cuboid or spheroidal cells which rest upon the membrana propria. They have an ovoid nucleus, rich in chromatin, and a small amount of cyto-

* Kölliker's Handbuch, III, 428.

plasm. Their cell outlines are often indistinct. These cells by mitotic division produce two daughter cells, one of which retains the structure and position of the mother cell, the other increases greatly in size and, assuming a more central position, becomes a spermatocyte. The subdivision of the spermatogonium marks the initial phase of spermatogenesis.

The spermatocytes, which arise by the division of the spermatogonia, are large cells. Their cytoplasm is finely granular, their nucleus large, and its rich supply of chromatin is arranged in a more or less skein-like manner. Because of the active mitosis oc-

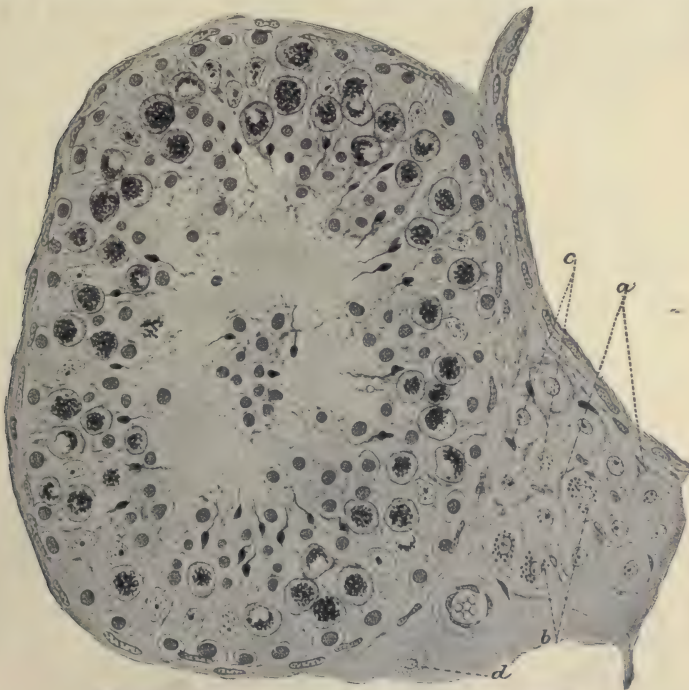


FIG. 306.—SEMINAL TUBULE OF A MAN IN TRANSECTION.

a and *b*, interstitial cells, the latter containing coarse granules; *c*, connective tissue cells; *d*, a mast-cell of the connective tissue. Within the tubule several phases of spermatogenesis are well shown. Highly magnified. (After Spangaro.)

curing in these cells their nuclear membrane is usually absent or indistinct. Mitotic figures are frequently observed in the spermatocytes. As a rule two divisions, resulting in two generations, occur in these cells; hence the frequency of the *double row* of large spermatocytes.

Mitotic division of the cells of the second generation or inner row of spermatocytes results in the formation of two spermatids. Hence each spermatocyte of the first order, producing two spermatocytes of the second generation, ultimately forms four spermatids, each of which is finally transformed into a spermatozoön. A peculiar fact in connection with this process is that in one of the mitotic divisions of the spermatocyte the chromosomes fail to divide in the ordinary manner, thus producing one-half the usual number of daughter chromosomes. This results in a reduction of the chromosomes during the spermatocyte stage to one-half the number elsewhere characteristic of the species. This "reduction" in the male germ, which is paralleled in the female during the development of the ovum, is of great importance in its relation to the processes of fertilization and maturation of the germ cell.

The spermatids formed by the division of the second generation of spermatocytes, are

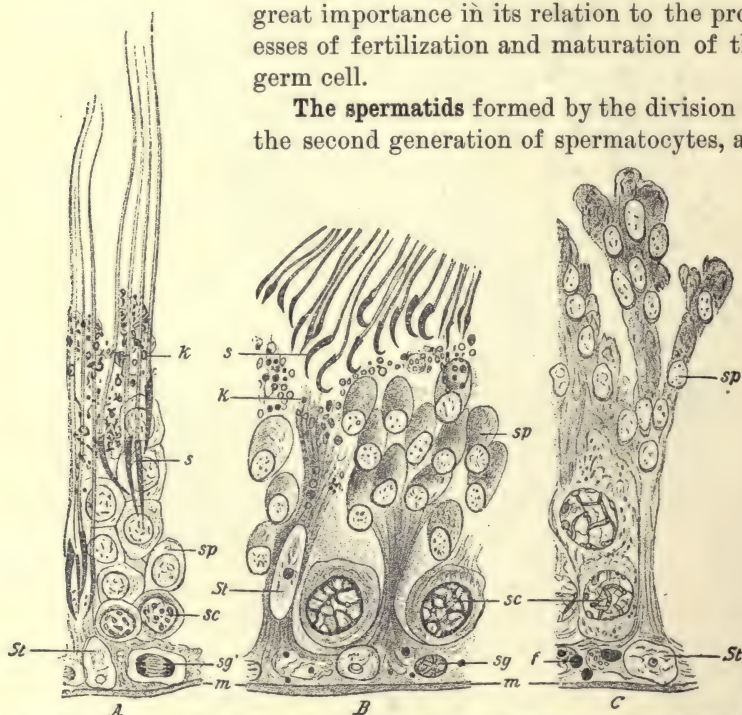


FIG. 307.—THREE PHASES OF SPERMATOGENESIS IN THE SEMINIFEROUS TUBULES OF THE RAT'S TESTICLE.

A, the formation of spermatosomes; B, discharge of the spermatosomes; C, formation of the spermatoblast; f, fat droplets, blackened by the use of a fixative which contained osmium tetroxid; k, fat and stainable granules; m, basement membrane; s, spermatozoa; sc, spermatocytes; sg, spermatogonia, in mitosis at sg'; sp, spermatids; St, cells of Sertoli. Saffranin. $\times 540$. (After K  lliker.)

small spheroidal cells with little cytoplasm and large spherical nuclei. Unlike the nucleus of the spermatocytes, that of the spermatid has a well defined nuclear membrane and its chromatin is distributed in irregular karyosomes. Mitosis is at an end; and each spermatid continues its development by direct transformation into a spermatozoön. At first the spermatids form an innermost group of independent cells; later they arrange themselves about the extremities of the Sertoli cells to which they become firmly united. In this way they enter into the formation of the spermatoblast of von Ebner.

The Sertoli cells are of large size and irregular columnar form. They possess an ovoid vesicular nucleus with a distinct nuclear wall and prominent nucleolus, but are otherwise poor in chromatin, a fact by which they can usually be distinguished from the neighboring cells, all of which are relatively rich in nuclear chromatin. The cytoplasm of the Sertoli cell is finely granular, toward the inner extremity often somewhat fibrillar; and the base of the cell frequently contains minute fat droplets. When first formed from the primordial cells, which also give rise to the spermatogonia, the Sertoli cells are cuboidal in shape and are relatively low; moreover, the long axis of their ovoid nucleus is nearly parallel to the basement membrane. As development proceeds and they unite with the spermatids to form the spermatoblasts, the Sertoli cells become greatly elongated, and their nucleus revolves until its long axis is nearly at right angles to its former position; it also becomes more centrally placed. The surface of their cytoplasm is indented by the attached spermatids and often presents short lateral processes by which the cell is placed in relation with a large number of the spermatid cells. As the spermatids develop into spermatozoa the heads of the latter cells become deeply embedded in the cytoplasm of the Sertoli cell, which is thus enabled to contribute to the cytoplasm of the spermatosomes. The tail pieces of the latter project centralward into the lumen of the tubule. Finally when the transformation of the group of spermatids into a corresponding number of spermatozoa is complete, the newly formed germ cells break away from the Sertoli cell and become free in the lumen of the seminiferous tubule.

The spermatids become spermatozoa by a process of direct transformation, the nucleus of the former producing the nucleus, and its cytoplasm the middle and tail pieces of the latter. In this process the nuclear chromatin becomes much condensed and

in the spermatozoön it forms a very dense compact mass. At the same time the cytoplasm is at first collected at one pole of the spermatid and then elongated to form the long flagellate tail of the spermatozoön. The middle piece of the spermatozoön seems to arise partly from the attraction sphere and partly from the cytoplasm of the spermatid.

The lumen of the seminiferous tubules is occupied by either the fully formed spermatozoa or by the developing tails of such of them as are still attached to the Sertoli cells, together with a scanty fluid secretion in which they are suspended, and numerous particles of granular débris which result from the degeneration of many spermatids which for some reason fail to develop into spermatozoa.

TUBULI RECTI

At the apex of the testicular lobule the tortuous seminiferous tubules pass into the rete testis of the mediastinum. At this point the tubule becomes straight and is abruptly narrowed. Thus the short straight tubules, tubuli recti, are formed. In the straight tubules the stratified epithelium of the tortuous portions is abruptly exchanged for a very low columnar or flattened type of epithelium with which the Sertoli cells of the tortuous tubules seem to be continuous. The straight tubules are very short and are soon transformed into the irregular anastomosing canals of the rete testis.

RETE TESTIS

The connective tissue of the mediastinum is permeated by a network of irregular channels of varying diameter which present frequent dilatations and often have the appearance of broad cleft-like spaces. These are the canals of the rete testis which form a dense network of anastomosing channels. On the one hand they receive the straight tubules, and on the other they pass into the ductuli efferentes, which convey the secretion onward to the globus major of the epididymis.

The canals of the rete testis are lined by cuboidal or flattened epithelium, which rests upon a delicate basement membrane. This in turn is supported by the connective tissue of the mediastinum. The broad but irregular lumen of the canals is occupied by the secretion from the seminiferous tubules and contains many spermatozoa.

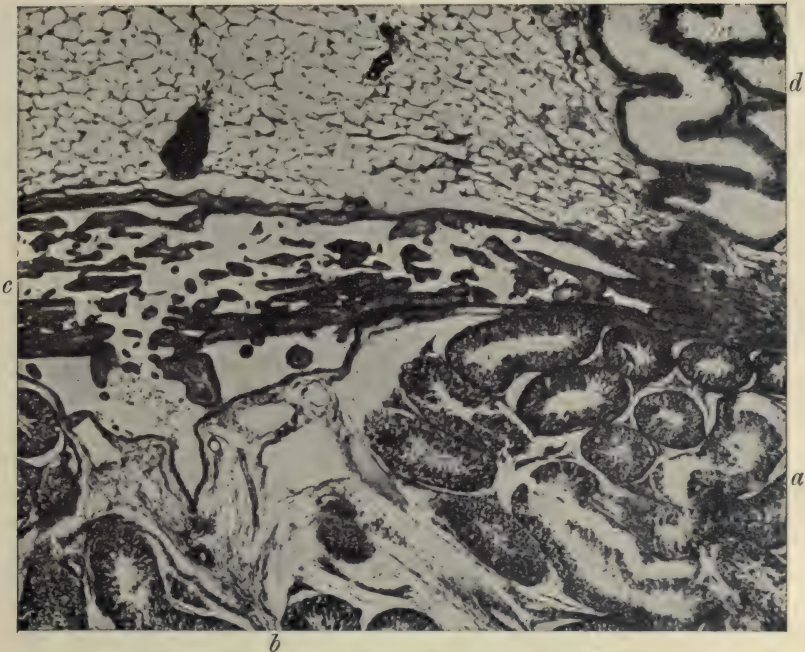


FIG. 308.—FROM THE DORSAL SURFACE OF A RABBIT'S TESTIS.

a, seminiferous tubules; *b*, mediastinum testis; *c*, rete testis; *d*, ductuli efferentes. Hematein and eosin. Photo. $\times 50$.

DUCTULI EFFERENTES

As the tubules of the rete testis leave the mediastinum they are abruptly transformed into peculiar efferent ducts, which pass into the globus major of the epididymis and by means of spiral windings form conical masses, *coni vasculosi*, whose apex projects into the globus major. The epithelium of these tubules is peculiar in that it contains two varieties of cells, and in that it is thrown into many prominent longitudinal folds or rugæ.

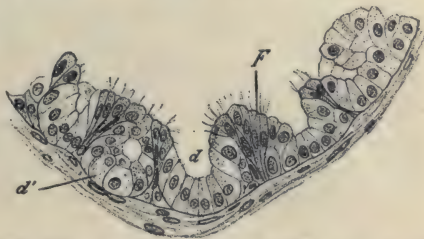


FIG. 309.—A SMALL PORTION OF THE WALL OF AN EFFERENT DUCTULE OF THE TESTICLE.

d, "glands" in longitudinal section; *d'*, the same in oblique section; *F*, ciliated epithelium. $\times 140$. (After Kölliker.)

In the lining epithelium there are short columnar cells which rest upon the basement membrane and carry upon their free ends

a tuft of short cilia. These cells have an ovoid nucleus and a very finely granular, eosinophile cytoplasm. Between and among the ciliated cells are many broad columnar or polyhedral cells,



FIG. 310.—EFFERENT DUCTULES OF THE RABBIT'S EPIDIDYMS.
Hematein and eosin. Photo. $\times 250$.

having remarkably clear cytoplasm, which chiefly occur between and at the base of the rugæ, and are frequently arranged in small groups simulating minute secreting glands. These clear cells have spheroidal nuclei and their cytoplasm is filled with large

coarse granules. They are quite characteristic of this portion of the excretory tubules of the testis. The *coni vasculosi* form a considerable portion of the *globus major* of the epididymis.

EPIDIDYMIS

The epididymis forms a long coiled tubule whose convolutions, by their regular cylindrical form and their tall ciliated epithelium, are sharply distinguished from those of the *ductuli efferentes*,

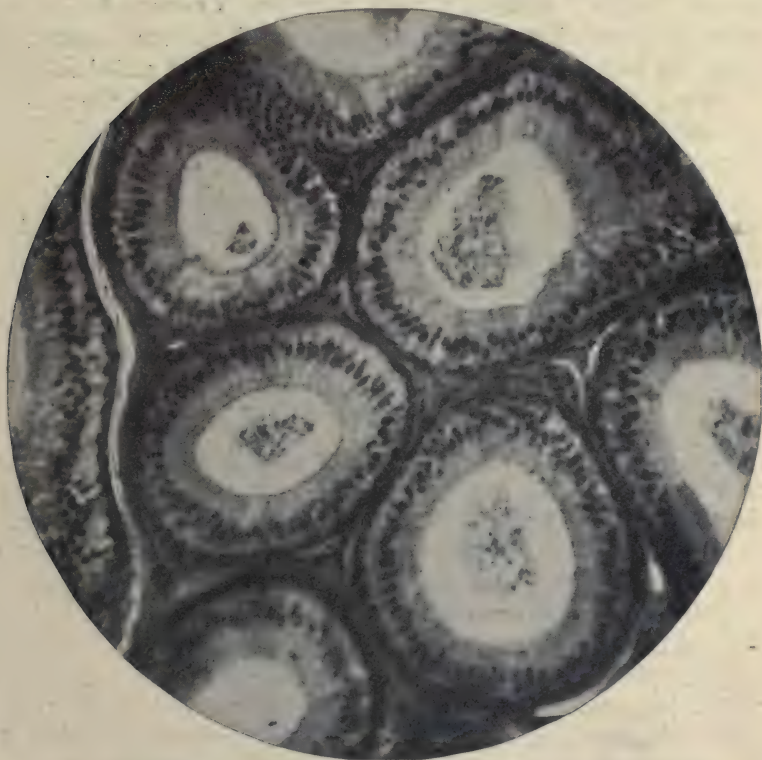


FIG. 311.—SEVERAL COILS OF THE RABBIT'S EPIDIDYMIS IN TRANSECTION.
The lumen of the tubules contains groups of spermatozoa. Hematein and eosin. Photo.
× 178.

which have much thinner walls. The lining epithelium of the epididymis is of the tall ciliated columnar type with elongated ovoid nuclei, a finely granular cytoplasm, and a group of cilia which often adhere together to form a peculiar tuft or cluster. At the base of the ciliated cells is an incomplete layer of basal

epithelium, whose flattened cuboidal elements are wedged between the bases of the tall columnar cells.

The epithelium rests upon a cellular basement membrane, which is supported by a connective tissue tunic of varying thickness. In addition to many elastic fibres, this coat contains a few smooth muscle cells (Klein *). The coils of the epididymis are firmly united into a solid mass by means of the dense intervening connective tissue. They form the whole of the globus minor and a considerable portion of the globus major. Connected with the canal of the epididymis near its junction with the vas deferens, or with the beginning of the latter tubule, is a short coiled tubular duct, which is found in the connective tissue between the epididymis and vas deferens. This is the *vas abberans* of Haller (see Fig. 303). It represents the remains of the fetal Wolffian duct.

The *appendix epididymis* and *appendix testis* (respectively the stalked and sessile hydatid of Morgagni) are formed by vascular folds of the tunica vaginalis, which in young individuals contain remnants of the Müllerian duct in the form of irregular tubules lined with columnar, rarely ciliated, epithelium. In the appendix testis they are frequently cystic.

THE VAS DEFERENS (*Ductus deferens*)

This duct is a continuation of the vas epididymis, whose course now becomes relatively straight. In this portion of the excretory duct of the testis the lining epithelium soon loses its cilia, and the basal cells become more prominent. Hence in the greater portion of its course the vas deferens is lined by tall, columnar, non-ciliated epithelium, with low basal cells between the attached ends of the columnar cells.

The epithelium rests upon a fibro-cellular basement membrane, which is supported by a fibrous tunica propria. This, in turn, passes almost insensibly into the muscular coat which consists of two layers, an inner circular and an outer longitudinal, both of which are highly developed. In the lower portions of the vas deferens, a thin internal layer of longitudinal muscle fibres is also found. The fibres of the internal and middle circular layers are frequently less regularly arranged, in which case their oblique bundles interlace with one another in a most intricate manner. The very thick, smooth muscular coat and the relatively narrow

* Stricker's Handbook, ii.

lumen give this portion of the duct a firm consistence and a cord-like feel.

In its ampulla the mucous membrane of the vas deferens is more loosely attached and the folds or rugæ, which elsewhere are few in number, are here very pronounced. The lumen of the ampulla is broad, but elsewhere the lumen of the vas is very

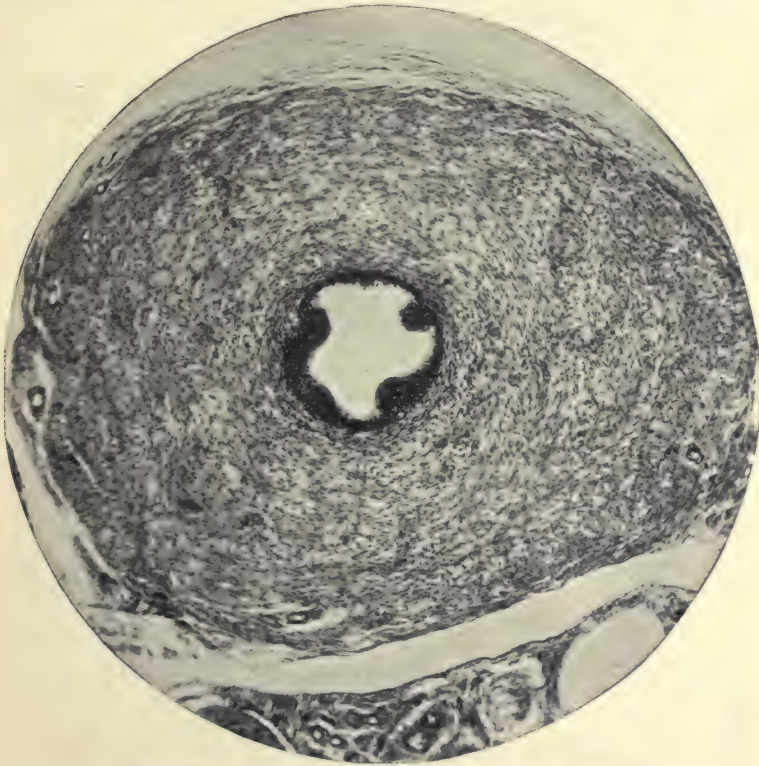


FIG. 312.—TRANSECTION OF THE VAS DEFERENS OF A DOG.

Hematein and eosin. Photo. $\times 104$.

narrow, especially when compared with its exceptionally thick muscular wall. As in other portions of the excretory canal of the testicle, the lumen of the vas deferens contains many spermatozoa.

The spermatic cord in its scrotal portion, in addition to the vas deferens, contains a mass of connective tissue in which are embedded the smooth muscle fibres of the internal cremaster muscle,

the spermatic artery, veins, and nerve plexus, the vessels of the pampiniform plexus, and the paradidymis or organ of Giralès. The whole is invested by a reflection of the tunica vaginalis.

The *pampiniform plexus* is a considerable group of venous spaces, usually completely collapsed after death, which are characterized by very thick, firm, fibro-muscular walls. The vessels are embedded in dense connective tissue, and the whole plexus in general appearance somewhat resembles the erectile tissues.

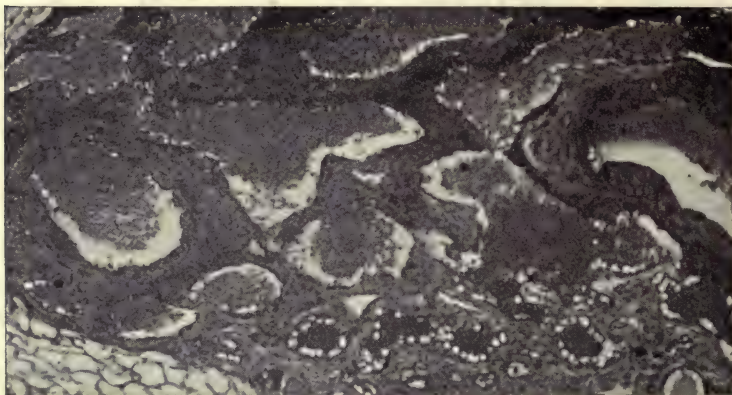


FIG. 313.—THE BLOOD VESSELS OF THE PAMPINIFORM PLEXUS OF A RABBIT.
Hematein and eosin. Photo. $\times 70$.

The *paradidymis* consists of a variable number of tubules which are lined by columnar epithelium and are regarded as fetal remnants of the Wolffian duct. They occur in relation with the vas deferens just above the level of the globus major of the epididymis.

THE SEMINAL VESICLES

The walls of the seminal vesicles consist of a thin outermost coat of connective tissue in which are many small ganglia, a muscular coat similar to that of the vas deferens but much thinner, and a characteristic mucosa. The tunica propria of the mucous membrane is a thin layer of delicate cellular connective tissue which loosely attaches the lining epithelium to the muscular coat. The surface of the mucosa presents numerous folds which not only form longitudinal rugæ but also possess an intricate network of secondary ridges which are both longitudinal and transverse in direction. This peculiar arrangement results in the appearance

of diverticula of various forms and sizes which, except that their epithelium does not differ from that of the surface, might often be interpreted, when seen in section, as representing secondary

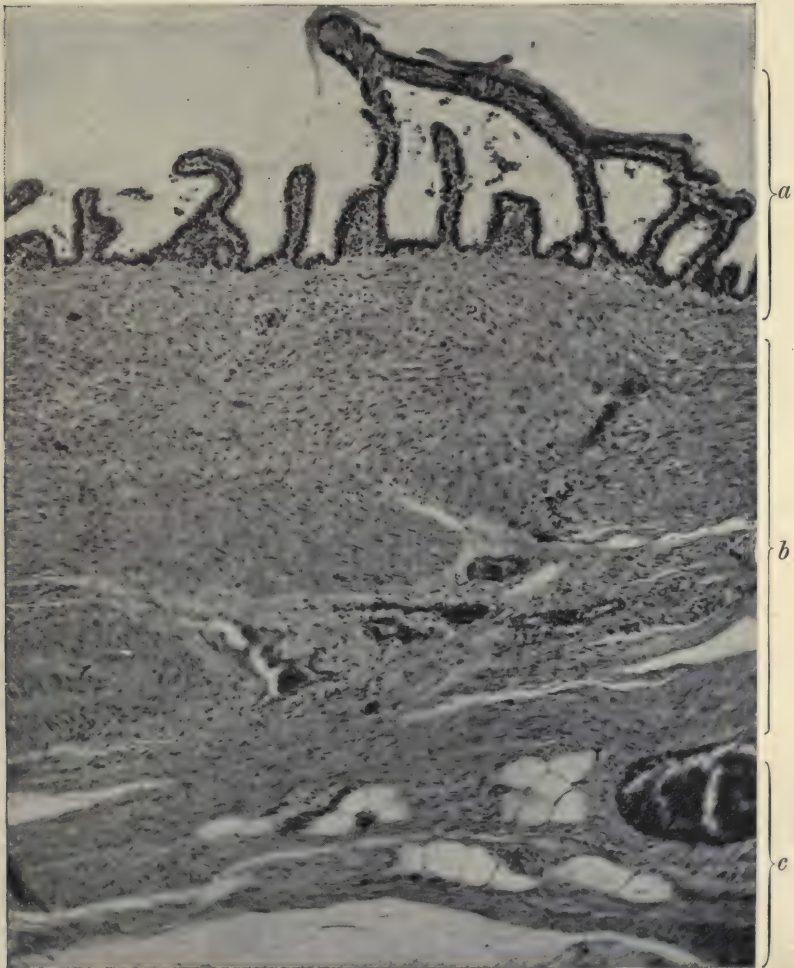


FIG. 314.—FROM A SECTION THROUGH THE WALL OF A SEMINAL VESICLE OF MAN.
a, mucosa; *b*, muscular coat; *c*, fibrous coat. Hematein and eosin. Photo. $\times 185$.

secreting glands within the mucosa. Slender processes of the corium extend into all the folds of the mucous membrane.

The lining epithelium of the seminal vesicles is of the colum-

nar type and usually contains but a single layer of cells. Occasionally basal cells are also found in the deeper part of the epithelial layer; in such case the epithelium may be said to be of the pseudo-stratified type. This variation may possibly be partly dependent upon the distention or relaxation of the vesicles. The cells of the epithelium contain peculiar granules of yellowish pigment which are present in considerable numbers and are quite characteristic of the organ. The superficial cells appear to be readily desquamated, and together with coarse granules of secretion form the chief contents of the lumen. Occasional small concretions of irregular form, and homogeneous or lamellar structure, similar to those of the prostate gland, are also found. The seminal vesicles usually contain but few spermatozoa. Occasionally these are present in larger numbers; at other times they may be entirely absent.

THE EJACULATORY DUCTS

These ducts are formed by the union of the ampullæ of the vasa deferentia and the ducts of the seminal vesicles and are similar in structure to the ampullæ of which they are the continuation. The ejaculatory ducts, however, possess a thinner wall and their mucosa presents the same folded condition as in the seminal vesicles, but to a lesser degree. In its prostatic portion the musculature of the vas deferens blends with the muscular stroma of the prostate, so that in the ejaculatory duct the smooth muscle no longer forms a distinctly lamellated coat. On approaching the urethra, the epithelium of the ejaculatory ducts presents a gradual transition to the stratified epithelium of the urethral canal.

THE PROSTATE GLAND

This is a compound tubulo-alveolar gland which pours its serous secretion into the neighboring portion of the urethra by means of two large and many small ducts. These open either directly into the urethral canal or indirectly through the utriculus prostaticus (sinus pocularis). The secreting alveoli are embedded in a very dense fibro-muscular *stroma* which, at the surface of the organ, forms an unusually thick *capsule* in which interlacing bundles of smooth muscle are most prominent. This portion of the stroma also contains intrinsic striated muscle fibres in limited numbers. Broad bands of fibro-muscular tissue pass inward from the capsule and form a network of thick septa in the meshes of

which are the glandular alveoli. These septa converge toward the urethra, which penetrates the ventral portion of the organ, their muscular fibres finally blending with the sphincter fibres of the prostatic portion of this canal.

The stroma consists of smooth muscle and connective tissue; their fibres are intimately blended. The muscle cells form either groups or bundles of variable size, or are frequently isolated within the meshes of the connective tissue. Their extreme abundance—in some parts exceeding the connective tissue in volume—is characteristic of the prostatic stroma. The connective tissue, which is sparingly supplied with elastic fibres, is rich in cells. Near the secreting alveoli, which possess no true wall other than their epithelium, the muscle fibres are absent and the cellular connective tissue becomes more prominent, thus forming a sort of tunica propria for the tubular alveoli.

The secreting epithelium is of the tall columnar type, sometimes forming a single, sometimes a multiple cell layer. Its cells possess spherical or ovoid nuclei which lie in their deepest third. Their cytoplasm is finely granular and often contains small yellowish granules. The epithelium rests directly upon the underlying connective tissue, the basement membrane being absent or but poorly developed. Wherever it is possible to demonstrate a *membrana propria*, it consists either of elastic fibres or of flattened connective tissue cells which are closely applied to the attached surface of the epithelium.

The epithelium is remarkably folded upon itself, the narrow interval between the two layers of the epithelial folds being always occupied by delicate extensions of the connective tissue stroma.



FIG. 315.—MODEL OF A RECONSTRUCTED PROSTATE GLAND OF MAN.

The figure includes one lobule. The narrow duct expands and terminates in a large number of alveoli of very varied size and form. $\times 40$. (After Maziarski.)

The prominence of the folds varies greatly in different tubules, some showing scarcely any such, the lumen of others being subdivided by deep rugæ into numerous anastomosing compartments.

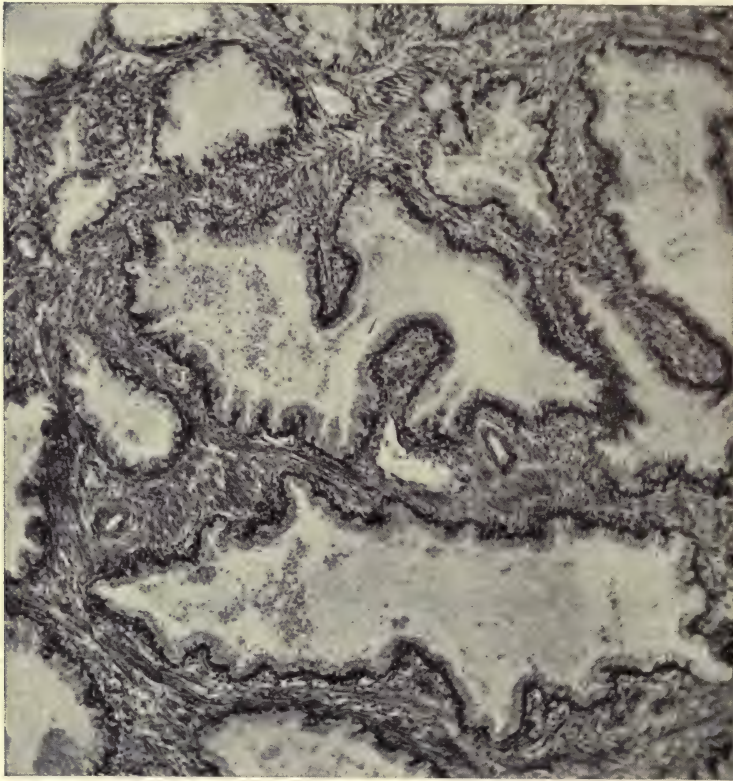


FIG. 316.—SEVERAL ALVEOLI OF THE HUMAN PROSTATE GLAND, SEEN IN SECTION.
Hematein and eosin. Photo. $\times 160$.

The amount of the folding also varies in different species, being more highly developed in some of the lower mammals, e. g., the dog, than in man.

The lumen of the prostatic tubules is broad, and is beset with numerous alveolar dilatations and shallow diverticula. It is usually broader near the blind extremity and diminishes somewhat in diameter toward the duct. The caliber of the lumen also varies greatly in different tubules and is possibly dependent in part upon the state of secretory activity. The contents of the lumen include

the granular albuminous secretion, desquamated epithelial cells, and, as age advances, many so-called *prostatic concretions*. The concretions vary greatly in size ($10\ \mu$ to 1 mm. in diameter), and may be homogeneous, but more frequently present a distinctly lamellated appearance. Prostatic concretions may occur at all ages but increase both in number and size in later life. Occasionally they attain a large size and may become encysted.

The prostatic ducts are lined by either a single or a pseudo-stratified layer of columnar epithelium, and, except for their narrower caliber and more regular contour, they closely resemble the secreting tubules. As the ducts approach their termination their epithelium increases the number of its cell layers. The larger ducts, just prior to their termination, are lined by transitional epithelium similar to that of the urethra, into which they open.

The prostate gland possesses a rich blood supply. Its larger vessels are found in the capsule, whence they send branches into all portions of the fibro-muscular stroma, and form a rich capillary plexus in the connective tissue layer about the epithelium of the secreting alveoli, and a second plexus in the substance of the stroma itself. The prostate is abundantly supplied, also, with lymphatic vessels, which are connected with the deep pelvic glands.

The capsule of the prostate, as also the neighboring connective tissue, both in relation with this organ and with the adjacent seminal vesicles, contains many nerve trunks and small ganglia. The latter are especially numerous. In this region a peculiar variety of special

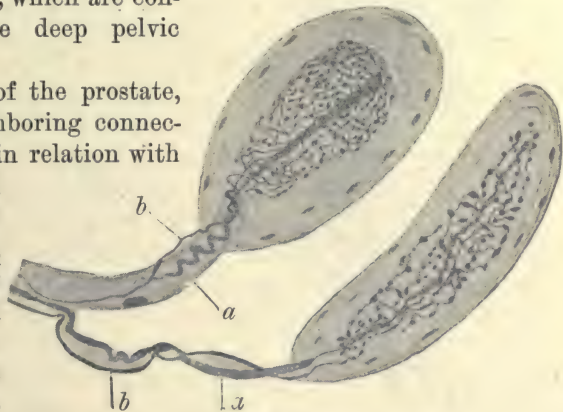


FIG. 317.—PROSTATIC GENITAL CORPUSCLES.

a, axial nerve fibre; *b*, peri-axial nerve fibre. Methylene blue. Moderately magnified. (After Timofejew.)

nerve ending is found. It was formerly regarded as a Paccinian corpuscle, but differs somewhat from these bodies. It perhaps more nearly resembles the *genital corpuscles*. These bodies are distinctly lamellated and possess a broad axial nerve fibre which

somewhat resembles that of the end bulbs of Krause. This nerve fibre is, however, accompanied by another and finer fibre which, as Timofejew* has shown, breaks into a close network of fine fibrils surrounding the axial nerve fibre in a peculiar basket-like manner.

THE BULBO-URETHRAL GLANDS (*Cowper's Glands*).

These are two small tubulo-acinar glands which are divisible into numerous small lobules. The lobules are separated by connective tissue septa containing both smooth and striated muscle fibres. The secreting acini are lined by columnar cells, some of which are finely granular and stain with eosin and acid dyes, while others are apparently filled with mucous secretion and react to the specific dyes for mucin. Certain other tubular alveoli are lined by low cuboidal or flattened epithelium. The epithelium rests upon a distinct cellular basement membrane.



FIG. 318.—RECONSTRUCTION OF A COWPER'S GLAND OF MAN.

The tubular ducts are closely surrounded by the expanded alveoli. $\times 100$. (After Maziariski.)

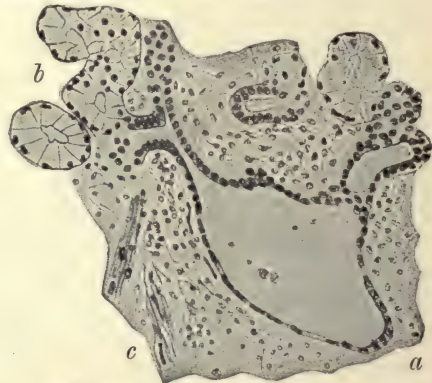


FIG. 319.—FROM A SECTION OF A COWPER'S GLAND OF MAN.

a, duct; b, tubules; c, stroma. $\times 130$. (After Braus.)

The intralobular and the smaller interlobular ducts are also lined by a single layer of columnar cells. Their wall is supplied with smooth muscle, most of whose fibres have a longitudinal direction. The two ducts of Cowper's glands open into the bulbous portion of the urethra.

* Anat. Anz., 1896.

CHAPTER XXI

THE FEMALE REPRODUCTIVE ORGANS

THIS system includes the ovaries, oviducts, uterus, vagina, and external genitals. All of these organs are concerned in the reproductive functions, produce the germ cell or ovum and provide a suitable site for its maturation and fertilization, and for the later development of the resulting embryo.

THE OVARY

The ovary is a solid ovoid body, attached to the margin of the broad ligament by a short, thick, connective tissue pedicle, the *mesovarium*, which transmits the blood vessels with which the ovary is richly supplied. At its ovarian attachment the mesovarium becomes continuous with the connective tissue stroma of the ovary. The indentation which is thus produced is known as the *hilum*.

The substance of the ovary is divisible into a central medulla which reaches the surface only at the hilum, and a peripheral *cortex* which invests all other portions of the medulla and is in turn clothed by a layer of *germinal epithelium*, a continuation of the peritoneal epithelium, whose cells in this area are peculiar in that they possess a typically cuboidal shape, and are thus sharply distinguished from the flattened endothelial cells of the surrounding portions of the peritoneum.

THE MEDULLA of the ovary consists of a fibro-muscular stroma and large numbers of blood vessels. Its arteries are characterized by their spirally tortuous course and thick muscular walls; its veins are numerous and large, and their endothelium rests almost directly upon the fibro-muscular stroma. This portion of the ovarian stroma consists of fibrous connective tissue in which are elastic fibres and considerable numbers of smooth muscle cells. The connective tissue is richly supplied with cellular elements, most of which are ovoid or fusiform in shape.

THE CORTEX of the ovary likewise contains a vascular stroma and also large numbers of ova which are in all stages of development, from the genetic cells of the germinal epithelium up to the more mature germ cells, contained within epithelial sacs and known as *Graafian follicles*. During the menstrual epoch the ovaries also contain peculiar yellowish bodies, *corpora lutea*, resulting from the rupture of the largest Graafian follicles, a phenomenon which marks the climax of the process of ovulation.

The stroma of the ovarian cortex is a connective tissue structure which contains relatively few elastic fibres and, except near the medulla, very little if any smooth muscle. It is, however, abundantly supplied with connective tissue cells of large size, most of which are ovoid, fusiform, or even considerably elongated in shape. Many of these cells closely simulate smooth muscle on superficial examination, but are readily distinguished by careful study, especially if specimens are prepared by the various differential staining methods.

In the vicinity of the Graafian follicles the stroma is specially rich in cellular elements and is otherwise modified to form a concentric coat for each of these bodies. This coat, the *theca folliculi*, consists of (a) an outer layer, or *tunica externa*, composed chiefly of connective tissue whose interlacing bundles are concentrically disposed, (b) an inner layer, *tunica interna*, which is peculiarly rich in large ovoid cells, and (c) an innermost *membrana propria*, upon which the epithelial cells of the follicle directly rest.

At the surface of the ovary the cortical stroma forms a dense layer of fine connective tissue fibres whose delicate bundles interlace in a close-meshed network. This layer, which immediately underlies the germinal epithelium at the surface of the ovarian cortex, is known as the *tunica albuginea*. It differs greatly in thickness in different mammalian species, in different individuals of the same species, and even in different portions of the same ovary. Its deeper surface blends insensibly with the underlying stroma of the cortex.

The general appearance of the ovary varies according to the number, size, and stage of development of its ova and Graafian follicles. At birth the cortex is packed with large numbers of newly formed ova, all of which are in approximately the same stage of development. During childhood the formation of larger follicles goes forward at an unequal rate, some ova rapidly approaching maturity, others apparently remaining almost stationary,

and still others undergoing retrograde development, so that at the age of puberty the ovary contains germ cells and follicles in all stages of development. After puberty the ripe follicles successively rupture and result in the formation of many corpora lutea which promptly degenerate, and are finally replaced by dense connective tissue in the form of small scar-like masses known as the *corpora albicantia*. Hence throughout the menstrual epoch the

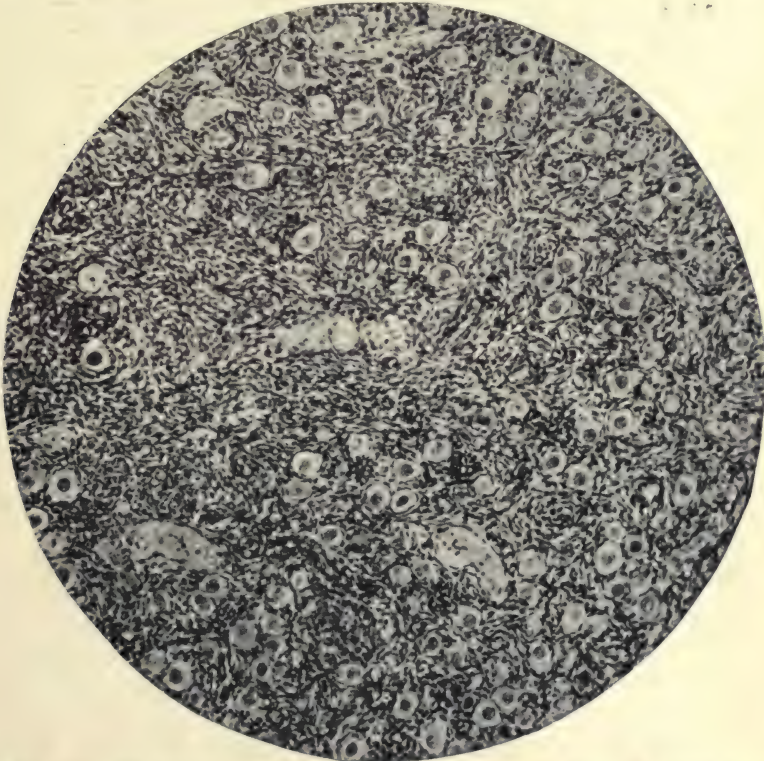


FIG. 320.—FROM THE OVARIAN CORTEX OF AN INFANT, SHOWING MANY OVA WHICH HAVE AS YET SCARCELY DEVELOPED TO EVEN THE EARLY STAGE OF A GRAAFIAN FOLLICLE. The portion above and to the right is near the free surface; that below and to the left adjoins the medulla. Hematein and eosin. Photo. $\times 200$.

ovarian cortex contains many corpora lutea and corpora albicantia in addition to ova and follicles in various earlier stages of development. It is doubtful, however, if during this period of life new ova are formed within the germinal epithelium, as occurs in infancy and childhood as well as during fetal life. After the climac-

teric the remaining follicles degenerate and the process of ovulation gradually ceases.

We shall now discuss the structure of the ovum or female *germ cell* and shall then successively trace its development and maturation, the formation of its Graafian follicle, the rupture of the follicle, and the subsequent history of the corpus luteum.

THE OVUM.—The ovum is a spherical cell of large size (200 to 300 μ). When fully developed it is surrounded by a thick layer of exoplasm, the *zona pellucida*, which is probably derived from the cytoplasm of the follicular epithelium by which the ovum is closely invested. The ovum itself consists of a mass of cytoplasm, the *vitellus*, and a large vesicular *nucleus* or *germinal vesicle*, within which is frequently a single prominent *nucleolus* or *germinal spot*. The cytoplasm of the mature ovum is inclosed by a very delicate cell membrane, known as the *vitaline membrane*, which is not demonstrable in the primitive ova of the younger follicles.

The **cytoplasm** of the ovum at first appears finely reticular, but as its development advances a fatty material is deposited within its meshes, usually in the form of minute irregular spheroids, by the accumulation of which the reticular cytoplasm is in great part replaced by a granulo-fatty mass of faint yellowish color known as *deutoplasm*. Frequently this metamorphosis is not quite complete, a remnant of the original cytoplasm persisting beneath the vitaline membrane and in the vicinity of the nucleus.

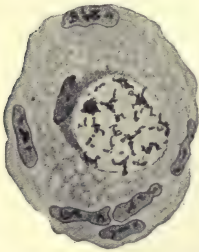


FIG. 321.—OVUM, CONTAINING A YOLK NUCLEUS (DOTTERKERN) AT THE LEFT AND ABOVE THE NUCLEUS.

The peripheral nuclei are derived from the adjacent stroma. Iron-haematoxylin. Highly magnified. (After von Skrobansky.)

Numerous cytoplasmic structures have been described in these cells, chief among which are the *accessory nucleus* (*Nebenkern*), and the *yolk nucleus* (*Dotterkern*). The accessory nuclei, occasionally chromatinic and therefore basophile, more frequently stain with cytoplasmic dyes and are at times attached, at other times separate from the true nucleus. The yolk nuclei of mammalian ova most frequently take the form of crescentic masses of lightly staining chromatin which partially surround the nucleus,

forming a so-called *nuclear cap*. They are often found in various stages of disintegration, and the fragments may be transported to the peripheral portions of the cytoplasm, or may be irregularly

scattered as small round chromatin granules, which occur throughout the cytoplasm. The physiological interpretation of these bodies is uncertain.

The nucleus of the ovum is a large spheroidal vesicle, the volume and distribution of whose chromatin is subject to great variation. Chromatin is present in greatest amount during the period of most active cell growth, in which the cytoplasm of the ovum is enormously increased in volume. At this time the nucleus often appears as a solid mass of chromatin. Later the chromatin is diminished in volume, portions of its substance being possibly extruded into the surrounding cytoplasm; the nucleus then acquires a characteristic vesicular appearance.

The nuclear membrane is sharply defined and is at most times prominent, except, as in other cells, during mitosis, a process which marks the final maturation of the germ cell. The nuclear matrix or nuclear sap abounds in the vesicular type of nucleus and the chromatin is scattered in small particles which adhere to the inner surface of the nuclear wall or to the delicate achromatic linin threads.

Each ovum as a rule contains a single nucleus (germinal vesicle), though occasionally two nuclei occur. The latter condition is presumed to arise either by the fusion of two ova within a single follicle or from incomplete cell division during development.

Each nucleus, during its vesicular stage, usually contains a single *nucleolus* (germinal spot), which forms a spherical mass of chromatin, situated, like the nucleus itself, eccentrically rather than centrally. The staining properties of the nucleoli vary remarkably. Usually they take the basic (nuclear) dyes to a greater or less depth; occasionally they exhibit an affinity for the acid (cytoplasmic) dyes; still other nuclei take a metachromatic or irregular tint with the ordinary nuclear stains. Many nuclei even in the absence of mitosis contain no nucleolus.

In the development of the ovum from the germinal epithelium, whose cells from their homology with the spermatogonia have been termed *oögonia*, there occur several mitoses which result in so-called *oöcytes*; these later develop into the complete ovum. At about the time of its extrusion from the Graafian follicle a final series of mitoses occur, which distinguish the maturation of the ovum. In this process there is a series of two mitoses which result in the appearance of the polar bodies and produce a *reduc-*

tion in the number of chromosomes to one-half the number which is characteristic of the somatic cells.* By the first mitosis the

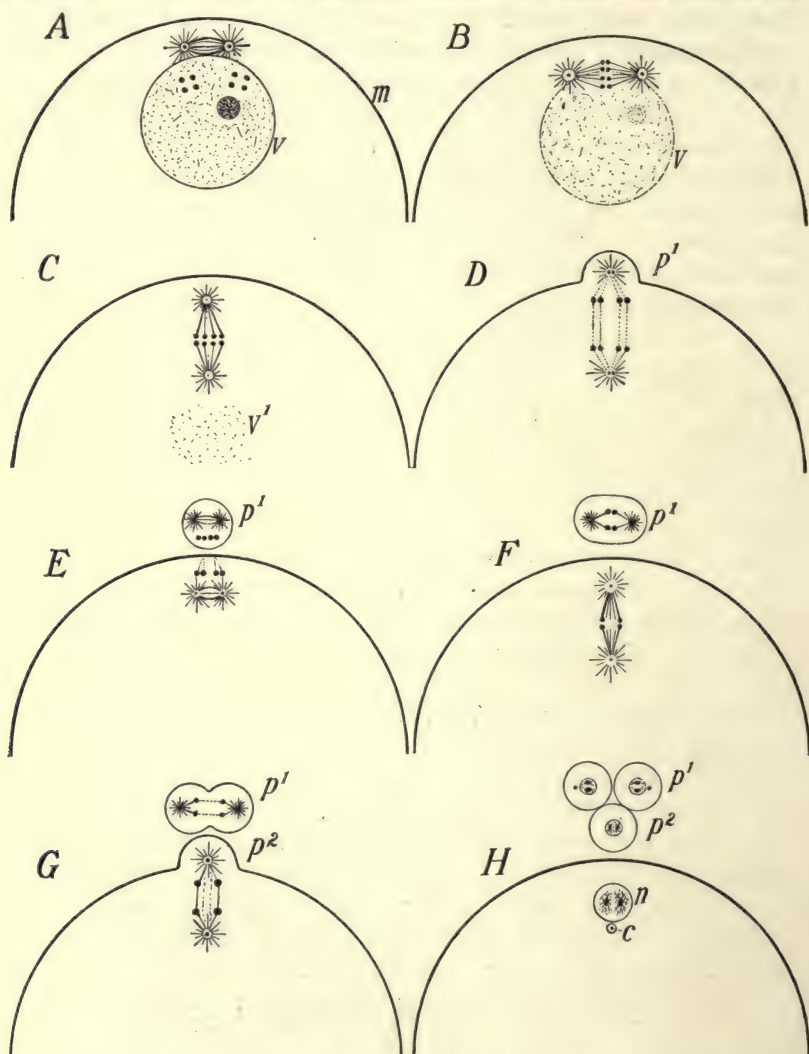


FIG. 322.—DIAGRAM OF REDUCTION DURING THE MATURATION OF THE OVUM.

A-H, successive stages; one-half of the cell, only, has been represented. c, centrosome; m, cell membrane; n, nucleus; p¹ and p², polar bodies formed in successive mitoses; V, germinal vesicle, which, at V¹, has nearly disappeared. The somatic number of chromosomes in the diagram is four; after reduction the germinal number is two.

* Body cells as distinct from the germ cells.

cell produces what may be termed a daughter ovum, together with the first *polar body*, a minute cell of insignificant size. The second mitosis is irregular in that the chromosomes separate without splitting, one-half going to the second polar body, the other to the mature ovum, thus effecting the reduction of the chromosomes, a deficiency which is compensated for in the event of fertilization by the entry and fusion of an equal number of chromosomes derived from the male sperm nucleus of the spermatozoon. The second mitosis may or may not be accompanied by mitotic division of the first polar body; in the former case three, in the latter only two polar bodies arise in connection with the process of maturation of the ovum.

DEVELOPMENT OF THE GRAAFIAN FOLLICLE

The development of the Graafian follicle goes hand in hand with that of the ovum and can be readily followed in ovaries from individuals of different ages, children and adults, the mature fol-

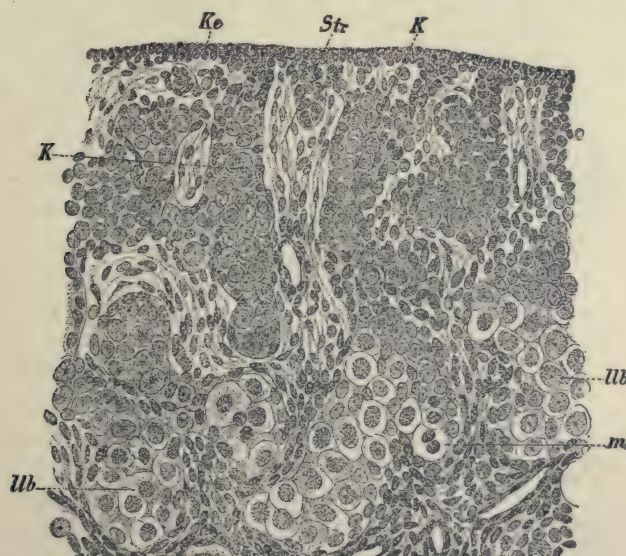


FIG. 323.—FROM A SECTION OF THE OVARIAN CORTEX OF A NEW-BORN KITTEN.

K, Pflüger's tubes; Ke, germinal epithelium; m, mitosis; Str, ovarian stroma; Ub, primitive follicles. Moderately magnified. (After Kolliker.)

licles and corpora lutea appearing only after puberty. The process begins in the germinal epithelium in which certain cells so increase in size that they may be readily distinguished as future ova. More

frequently, however, the earliest step in the process consists in the growth of solid cell columns from the layer of germinal epithelium into the cortical stroma of the ovary. These cell columns are known as *Pflüger's tubes*, though, except occasionally at the extreme surface of the organ, they lack a true tubular form and possess no vestige of a lumen.

Certain cells in these columns, by their increased size and prominent nucleus, become very early distinguished as the primitive ova; their differentiation is rapidly followed by the constriction of the columns, through the activity of the surrounding tissue of the stroma, in such a manner that one, rarely two or more ova, and several undifferentiated epithelial cells are included in each portion whose connection with the layer of germinal epithelium is thus severed. In this way the *primitive follicles* (*egg nests*, or *Eiballen*) are formed. In the ovary of the new-born hundreds of such immature follicles occur in all portions of the cortex (Fig. 320). They are also found in large numbers in the ovary of the adult, though it is asserted that during adolescence their formation gradually ceases.

Many follicles never go beyond this primary stage of development, but after a time undergo retrograde metamorphosis either by gradual atrophy or by a process, known as *atresia* of the follicle, in which the chromatolysis in the ovum and its surrounding follicular cells is followed by growth and organization of the theca folliculi, the connective tissue which is thus formed finally replacing the atresic follicle.

After remaining stationary for a long period, often for years, certain of the primitive follicles enter upon a period of rapid growth. This process first affects the ovum and results in the appearance of the deutoplasm, zona pellucida, and other accessory structures, as already described under the development of the germ cell. Cell multiplication now occurs in the surrounding epithelial cells, so that, instead of the single row of epithelium which surrounds the ovum of the primitive follicle, the ripening follicle soon acquires a layer of follicular epithelium several cells deep.

The rapid multiplication of the epithelial cells is soon followed by active secretion, resulting in the formation of a clear fluid by which the cells are more and more separated, and the cytoplasm of adjacent cells is then readily seen to be firmly joined together by numerous delicate processes which may be regarded as *intercel-*

lular bridges. Similar processes unite the neighboring cells to the zona pellucida which has already formed about the ovum.

The accumulation of the fluid *liquor folliculi* within the follicle soon appears to tear apart certain of the epithelial cells, and a fluid-filled space, the *antrum folliculi*, is thus formed. This space is characteristic of the true Graafian follicle. The epithelial cells are separated by the antrum into two layers: the one, adherent to the membrana propria of the follicle, is known as the

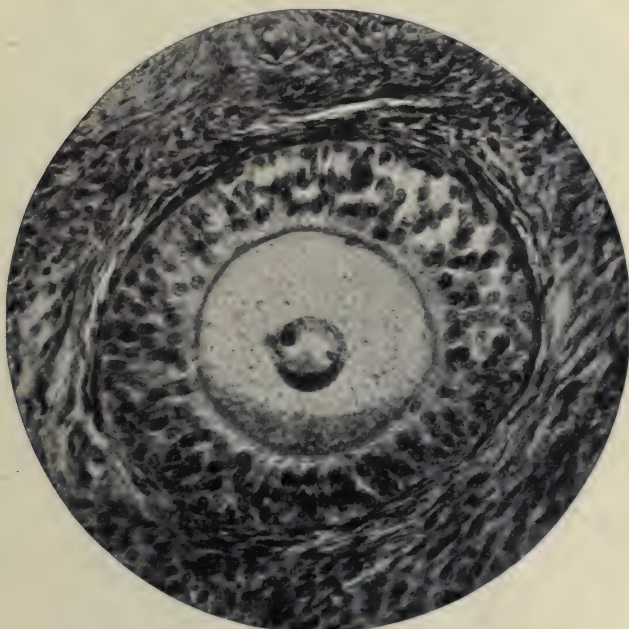


FIG. 324.—A GRAAFIAN FOLLICLE OF THE HUMAN OVARY.

From within outward are seen the germinal spot, germinal vesicle, vitellus, vitelline membrane, zona pellucida, granule cell layer, membrana propria, and theca folliculi. The ovarian stroma forms the border of the figure. Hematein and eosin. Photo. $\times 575$.

membrana or *stratum granulosum*; the other, adherent to the zona pellucida of the ovum, is designated the *discus proligerus*. The two layers remain in contact at one point, and as the liquor folliculi increases in volume, the attached discus proligerus with its contained ovum comes to occupy a more and more eccentric position, and the cells of the stratum granulosum, where the two layers are in contact, appear to pile up about the ovum in the form of a hillock, the so-called *cumulus oöphorus*.

The cells of the discus proligerus, which adjoin the zona pellucida, become somewhat elongated and in this way they form a radiate investment consisting of one or two rows of columnar cells which surround the zona pellucida of the ovum and are known as

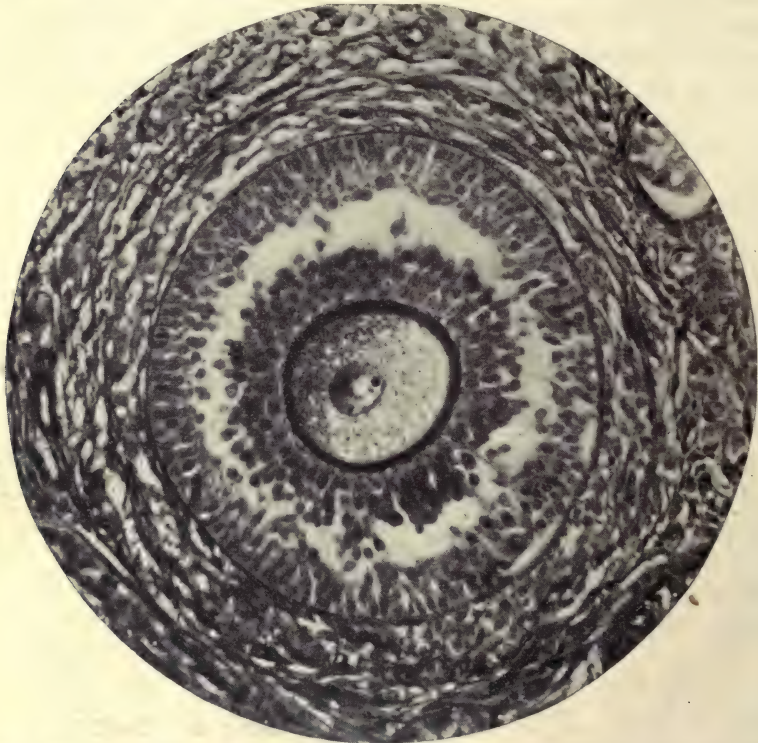


FIG. 325.—A GRAAFIAN FOLLICLE OF THE HUMAN OVARY, SOMEWHAT MORE ADVANCED THAN THE PRECEDING.

The accumulation of liquor folliculi has separated the granular cells into a discus proligerus and a membrana granulosa. The membrana propria is very sharp, and the theca folliculi is almost divisible into an inner cellular and an outer fibrous layer. Hematein and eosin. Photo. $\times 460$.

the *corona radiata*. With the increase of the liquor folliculi the discus proligerus with its contained ovum is soon separated from its attachment to the stratum granulosum and the development of the folliculi is complete.

During this period of rapid growth and development the follicle has increased in size from a diameter which scarcely exceeded that of its ovum (about $300\ \mu$) to such a size that it occupies

the entire breadth of the ovarian cortex. It is now ready for the final steps in the maturation of its ovum and for the rupture of the follicle coincident with the approach of the menstrual period.

The forces which lead to the rupture of the follicle are not fully determined. They are undoubtedly varied, and, in addition to the gradual attenuation of the layer of cortical stroma which covers the free surface of the follicle and is known as the *stigma*, they

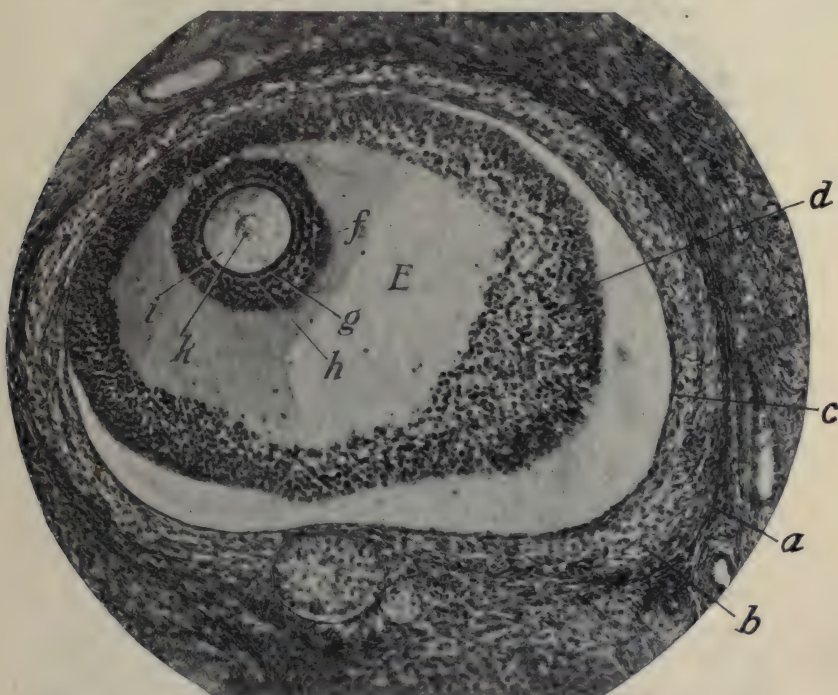


FIG. 326.—A NEARLY MATURE GRAAFIAN FOLLICLE FROM THE OVARY OF A DOG.

a, fibrous, and *b*, cellular layer of the theca folliculi; *c*, membrana propria; *d*, membrana granulosa, which, as a result of contraction during hardening, has retracted from the membrana propria, leaving a broad artificial space; *E*, liquor folliculi; *f*, discus proligerus; *g*, zona pellucida; *h*, vitelline membrane; *i*, vitellus; *k*, the germinal spot, lying within the germinal vesicle. Hematein and eosin. Photo. $\times 150$.

include the gradual accumulation of liquor folliculi under increasing tension, the marked congestion of the ovary at the approach of the menstrual period, which is accompanied by the determination of an undue proportion of blood to the theca of the ripe fol-

licle (Clark *), and possibly the contraction of the smooth muscle contained in the stroma of the deeper part of the cortex and adjacent portions of the medulla. In any event, as a result of the independent or combined action of these, or other unknown forces,

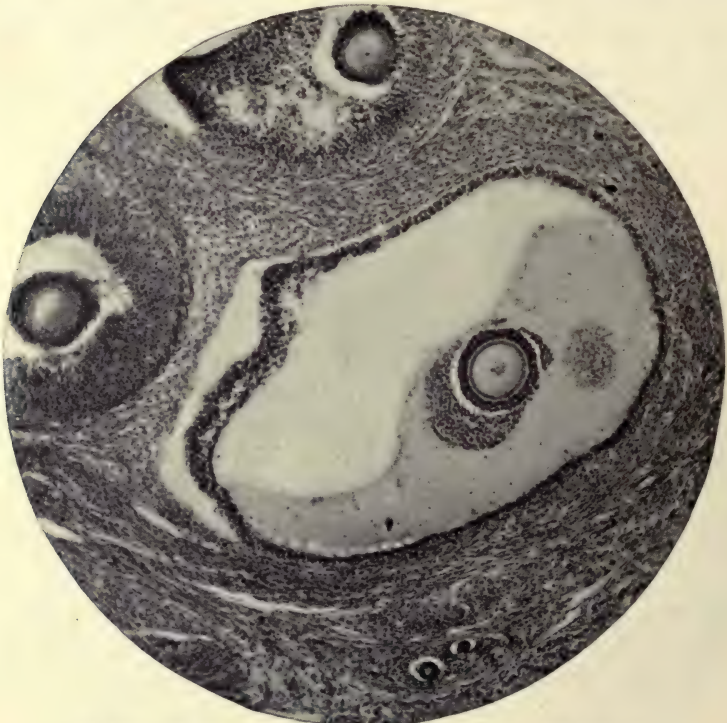


FIG. 327.—A MATURE GRAAFIAN FOLLICLE OF THE DOG'S OVARY.

Two smaller follicles are partially included in the figure. Hematein and eosin.

Photo. $\times 110$.

the follicle ruptures in the direction of least resistance, viz., at the attenuated stigma, and the liquor folliculi gushes forth, carrying with it the detached ovum invested with its discus proligerus. The ovum is now free to enter the oviduct and prepare itself for fertilization and the development of the future embryo.

The following table is offered for the benefit of the student as a *résumé* of the several structural layers of the mature Graafian follicle. The structures are enumerated in order from without inward :

* Contributions to the Sc. of Med., 1900.

- | | | |
|--------------------|---|-------------------|
| 1. Theca folliculi | { | tunica externa |
| | | tunica interna |
| | | membrana propria. |
2. Stratum (seu membrana) granulosum.
 3. Liquor folliculi—occupying the atrium folliculi.
 4. Discus proligerus.
 5. Corona radiata.
 6. Zona pellucida.
 7. Perivitelline space (possibly an artefact).
 8. Vitelline membrane.
 9. Vitellus.
 10. Nucleus or germinal vesicle.
 11. Nucleolus or germinal spot (if present).

The Corpus Luteum.—The rupture of the follicle is accompanied by sudden relief of the intrafollicular tension and consequent hemorrhage from the thin-walled capillaries of the theca folliculi. Thus the cavity of the follicle is filled with blood; the ruptured follicle is then known as a *corpus hemorrhagicum*. This is the first stage in the formation of the corpus luteum.

Promptly succeeding the formation of the corpus hemorrhagicum, *lutein cells* appear at the periphery of the body. They are large, ovoid or polyhedral cells having a clear finely granular cytoplasm and a peculiar yellow color due to the presence of a pigment known as *lutein*. Moreover, the cytoplasm of the lutein cells becomes very rapidly infiltrated with droplets of fat, likewise deeply colored by the lutein pigment which is apparently held in solution. The origin of these cells is somewhat obscure. By certain observers they have been thought to result from the growth and multiplication of those cells of the stratum granulosum which remain after the rupture of the follicle (Bischoff, Pflüger, Sobotta); by others they are derived from the connective tissue cells in the tunica interna of the theca folliculi (Kölliker, His, Palladino).

The lutein cells increase rapidly both in number and in size, and gradually encroach upon the margin of the blood clot whose progressive absorption precedes the advance of the lutein cells. But not only does the lutein mass grow centralward, it also, and especially in the event of fertilization of the discharged ovum with the consequently increased vascularity of the reproductive organs, grows at the periphery and in this way greatly increases the diameter of the corpus luteum.

Minute vascular sprouts of embryonic connective tissue now penetrate the lutein mass from the adjacent stroma of the theca folliculi, and growing centralward in septa-like processes, finally penetrate as far as the central blood clot. Hence the corpus luteum at this stage presents a more or less radiate structure. The central ends of the embryonic connective tissue septa fre-

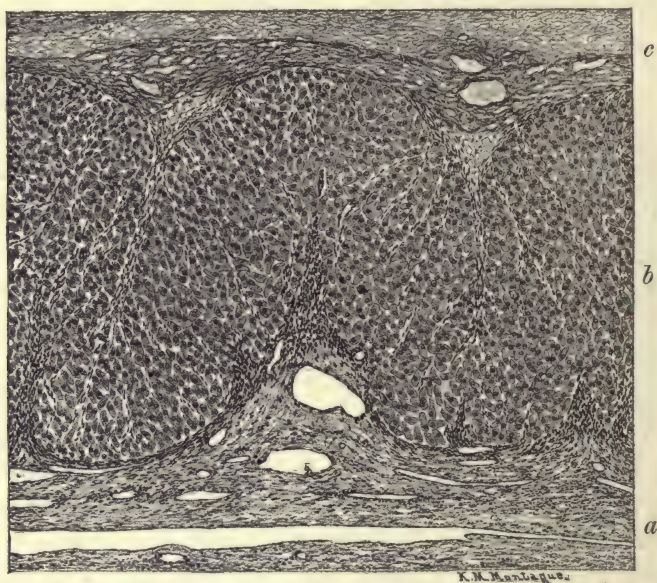


FIG. 328.—SECTION THROUGH THE PERIPHERAL PORTION OF A CORPUS LUTEUM, SHOWING LUTEIN CELLS.

a, the fibrous coat of the corpus luteum; *b*, lutein cells with bands of newly formed connective tissue; *c*, central blood clot, partially organized. Moderately magnified. (After Williams.)

quently unite to inclose the remnant of the central blood clot, or by further proliferation they may entirely replace the clot by a mass of newly formed gelatinous connective tissue.

The absorption of the blood clot usually proceeds slowly. Remnants of the disintegrating blood in the form of a central stellate mass, which often contains hematoidin crystals, frequently persist until the corpus luteum has become well organized with connective tissue.

The formation of new connective tissue is followed by its contraction. That this process occurs very early in the connective tissue first formed at the periphery of the body, may possibly be

held to account for the fatty infiltration and final degeneration of the lutein cells, because of the consequent interference with their vascular supply.

By continued development the entire mass of lutein cells is

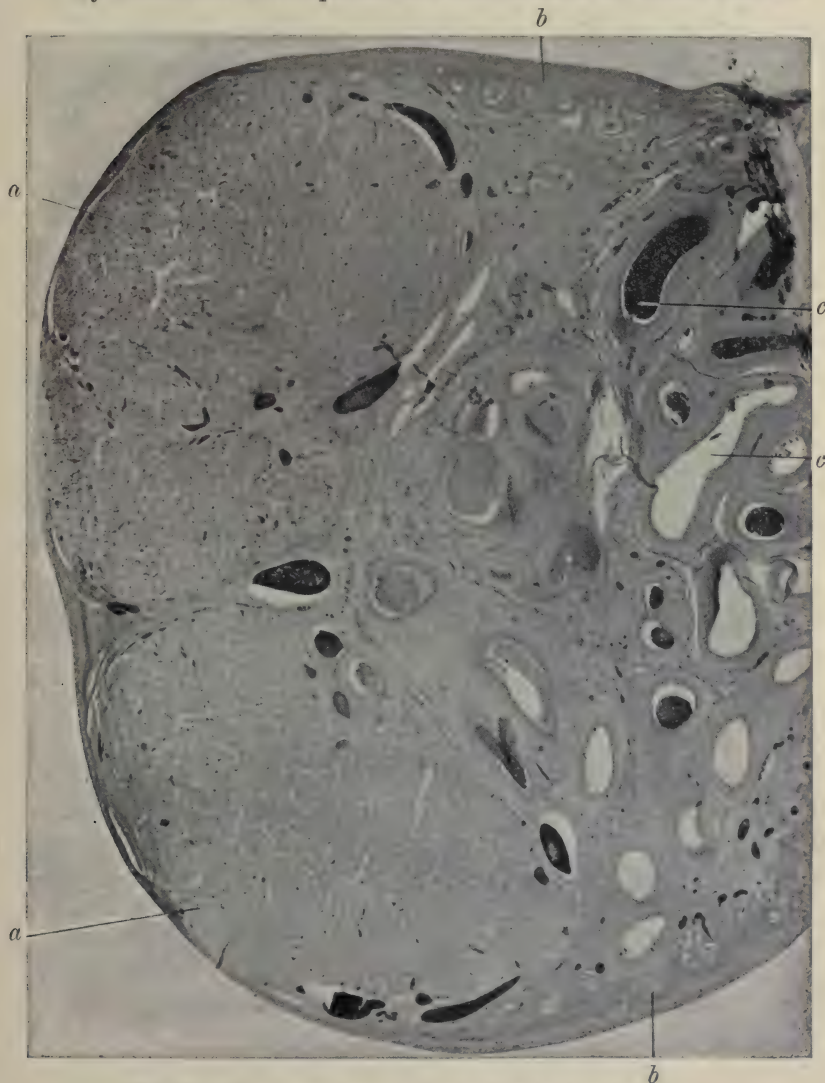


FIG. 329.—ORGANIZED CORPORA LUTEA IN THE OVARY OF A DOG.

a, a, corpora lutea; *b, b*, remnants of the ovarian cortex; *c, c*, blood vessels, one of which is filled with blood. Hematein and eosin. Photo. $\times 12$.

gradually replaced by connective tissue, which, by further contraction, finally produces a dense white fibrous *scar*, no longer containing lutein pigment, known as a *corpus albicans*. This body persists for a long period, but undergoes progressive contraction

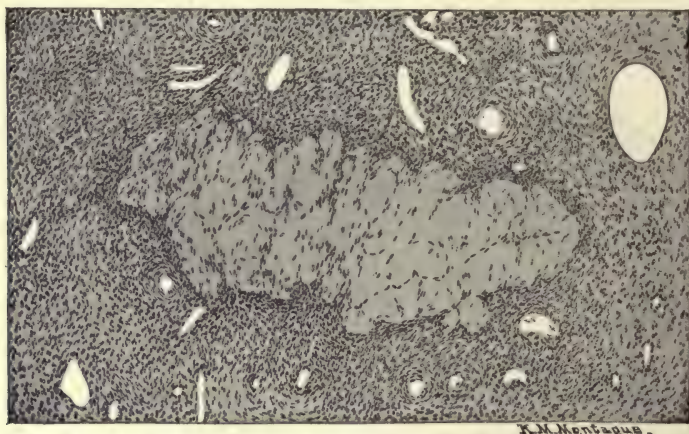


FIG. 330.—A CORPUS ALBICANS, FROM A SECTION OF THE HUMAN OVARY.
× 75. (After Williams.)

until only a minute scar of almost microscopical size remains to mark the site of the ruptured corpuscle and the highly developed corpus luteum. Such scars persist for years in the stroma of the ovarian cortex.

The function of the corpus luteum is practically unknown. A glandular function resulting in the formation of an internal secretion has recently been attributed to it (Born,* Cohn †).

Finally it must be stated that there are no recognizable histological differences, other than those of size and duration, between the *corpora lutea vera* of pregnancy and the *corpora lutea spuria* whose formation accompanies the extrusion of the unfertilized ovum. The true corpora lutea are of relatively large size and persist for many months, the spurious are somewhat smaller and are of shorter duration; yet both pass through the same histological process of development and degeneration and both leave their scars in the substance of the ovarian stroma.

Ovarian scars also arise through atresia of the larger follicles, the degeneration of whose epithelium is followed by an ingrowth of tissue derived from the theca folliculi, and the gradual develop-

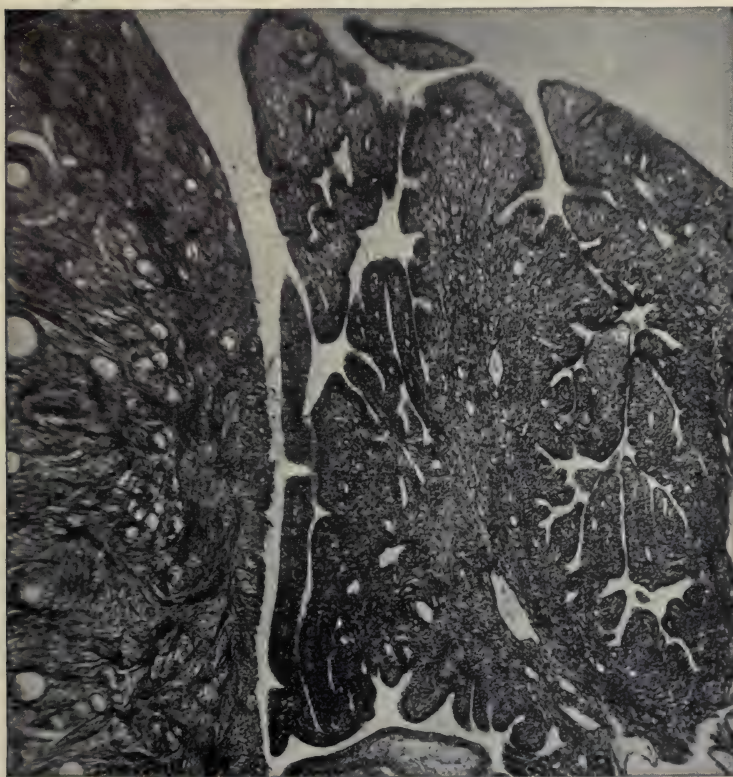
* Arch. f. mik. Anat., 1894.

† Ibid., 1903.

ment, organization, and final contraction of the connective tissue, forming, as it were, a minute but imperfect corpus albicans, in the center of which is often the shrunken degenerating remains of the ovum.

THE EPOÖPHORON.—In the margin of the mesovarium at its attachment to the medulla of the ovary, lies a peculiar structure which is variously known as the *epoöphoron*, *organ of Rosenmüller*, or *parovarium*. This structure is at present without

a



a

FIG. 331.—THE EPOÖPHORON OF A DOG.

a-a, margin of the ovary. Hematein and eosin. Photo. $\times 130$.

known function; it apparently represents the remains of the fetal Wolffian body and is homologous with a portion of the epididymis in the male.

The peritoneal epithelium in the region of the epoöphoron is



again thickened so as to acquire a columnar form, and from its surface, tubules and irregular invaginations extend into the substance of the mesovarium as far as its attachment to the broad ligament. Occasionally they extend well into the interior of the ligament and there form

a group of anastomosing channels,

a *rete ovarii*.

The tubules of the epoöphoron are lined by cuboidal or columnar epithelium whose cells are sometimes provided with cilia.

The epithelium rests upon a delicate mem-

brana propria and a

thin connective tissue tunic.

Blood Supply.—The blood vessels of the ovary are derived from the branches of the ovarian and uterine arteries. These vessels enter the ovary through the mesovarium and divide

FIG. 332.—FROM A THICK SECTION OF THE OVARY OF A WOMAN.

The blood vessels have been injected. A, a, and a', arteries; b, corpus luteum, partially organized; c, point where rupture of the follicle occurred; d, tangential section of a follicle; e, corpora lutea which have organized and are already retrogressive. (After Clark.)

into numerous branches which pursue a peculiar spiral or corkscrew course through the stroma of the medulla, and finally enter the cortex. They possess thick muscular walls containing bundles of longitudinal smooth muscle fibres. In the cortex they supply capillaries to the stroma, and in the theca folliculi of the Graafian follicles they form rich plexuses of broad capillaries and thin-walled venules. As the follicle approaches maturity these plexuses become enormously developed and apparently bear an important relation to the rupture of the follicle and the rapid development of the corpus luteum (Clark *). The veins, which take origin from the venules of these capillary plexuses, converge toward the medulla, where they form a plexus of large thin-walled vessels, the *plexus venosus ovarii* or *pampiniform plexus*, which is imbedded in the connective tissue of the medulla, the mesovarium, and the adjacent portions of the broad ligament.

The lymphatics arise in the cortical stroma by anastomosing canals and capillaries of irregular caliber, which are especially abundant in the walls of the Graafian follicles. These vessels converge toward the medulla, where they enter lymphatics which are supplied with valves, and find their way to the lymphatic nodes of the pelvic and lumbar regions.

The nerves are chiefly derived from the ovarian plexus. They enter the hilum and are distributed to the walls of the blood vessels, and to the stroma of the ovary; here they form a rich terminal plexus in the walls of the follicles. Whether or not the naked fibrils are distributed to the epithelial cells within the follicle has not been satisfactorily determined.

THE OVIDUCT

The oviduct or Fallopian tube is a narrow duct leading from the ovary to the cavity of the uterus. It consists of a broad, funnel-shaped, fringed or *fimbriated extremity*, a constricted *neck*, an intermediate *ampulla* of considerable diameter, and a slender *isthmus* by which the oviduct communicates with the uterine cavity.

Throughout the entire tube its wall consists of three coats—mucous, muscular and serous—but the character of its mucous membrane differs somewhat in its several portions. In the isthmus it is relatively smooth and usually presents four longitudinal ridges which have few secondary or accessory folds; in the ampulla the

* Contributions to Sc. of Med., 1900.

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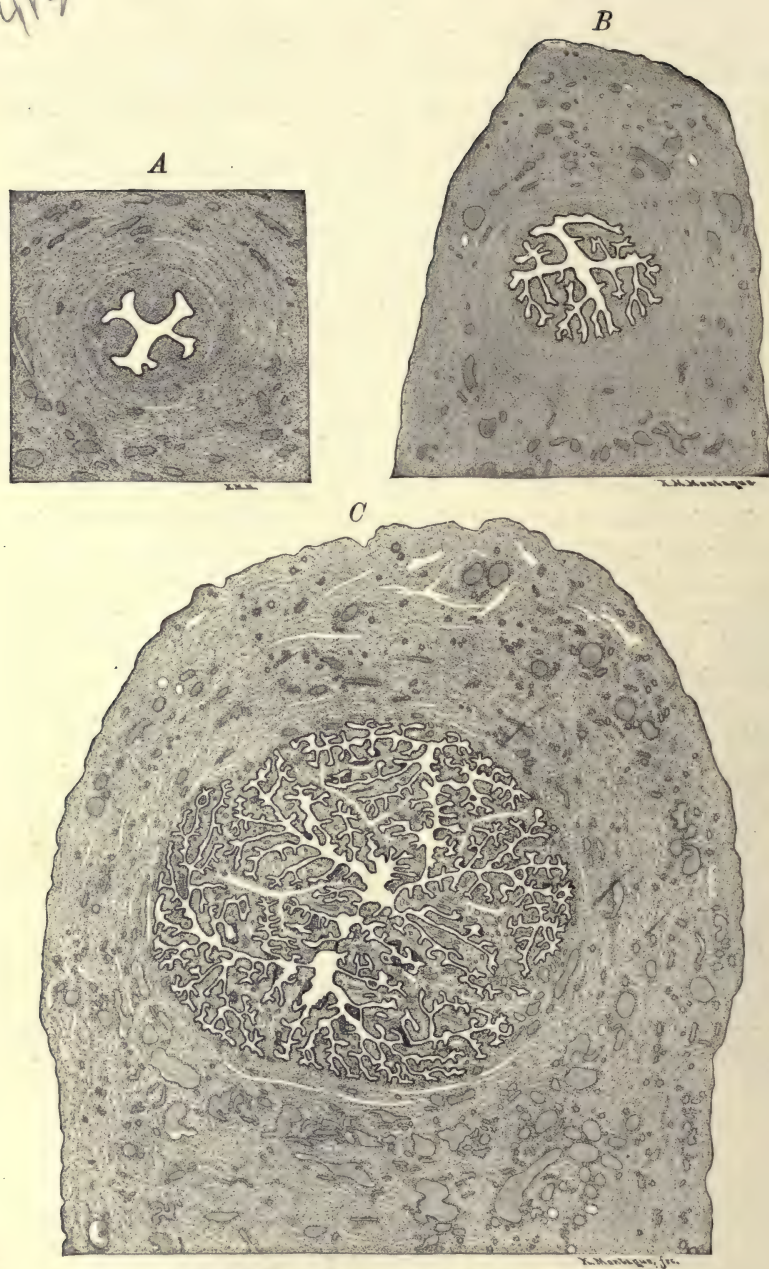


FIG. 333.—TRANSECTIONS OF THE HUMAN OVIDUCT.

A, uterine; B, isthmic; and C, ampullar portions. $\times 15$. (After Williams.)

mucosa is greatly folded, the primary rugæ possessing small secondary folds which extend in all directions, and by their very complexity nearly obliterate the otherwise broad lumen. In the fimbriated portion the folds of the mucosa are continued into the fimbriæ, at the margin of which the columnar epithelium of the oviduct becomes directly continuous with the serous endothelium of the peritoneum investing the outer surface of the tube.

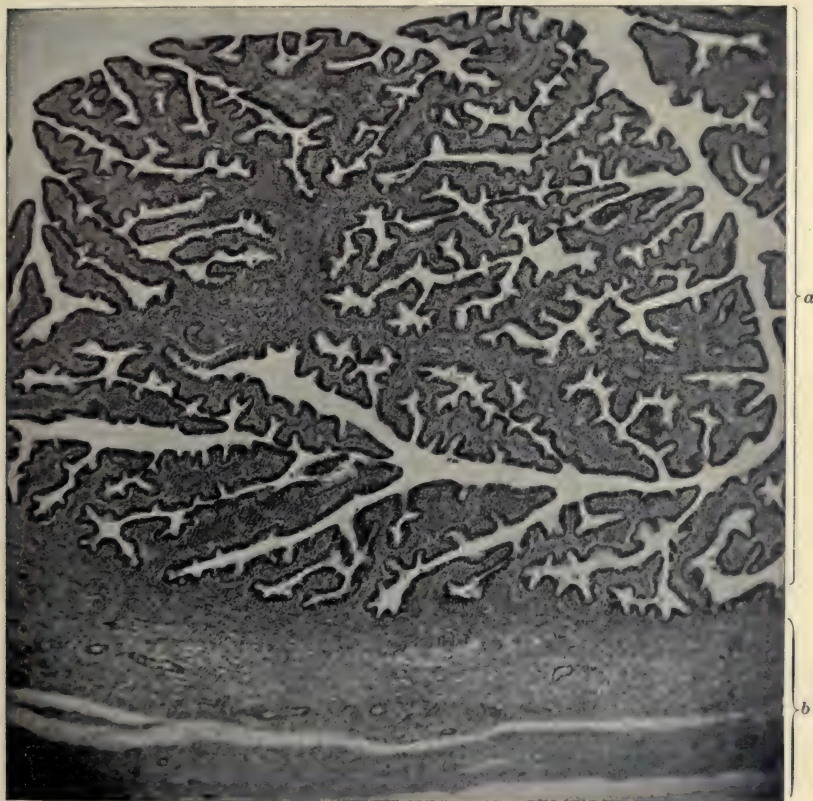


FIG. 334.—FROM A TRANSECTION OF THE AMPULLA OF THE HUMAN OVIDUCT.
One of the four major folds is included in the figure. *a*, mucosa; *b*, muscular coat.
Hematein and eosin. Photo. $\times 33$.

The mucosa is lined by columnar epithelium, arranged either in a simple or pseudo-stratified manner, the greater portion of whose cells are provided with cilia. The ciliary motion is directed toward the uterus. The epithelial layer covers all the folds of the mucosa

and, extending deeply into the crevices, forms invaginations which, in transections of the tube, simulate glandular structures. There are, however, no true secreting glands in the oviduct.

Here and there groups of non-ciliated cells with clear cytoplasm occur among the more numerous ciliated cells of the mucosa. This arrangement reminds one of the epithelium of the early portion of the epididymis with which the oviduct is homologous.

The epithelium rests upon a thin homogeneous basement membrane beneath which is a tunica propria consisting of a cellular

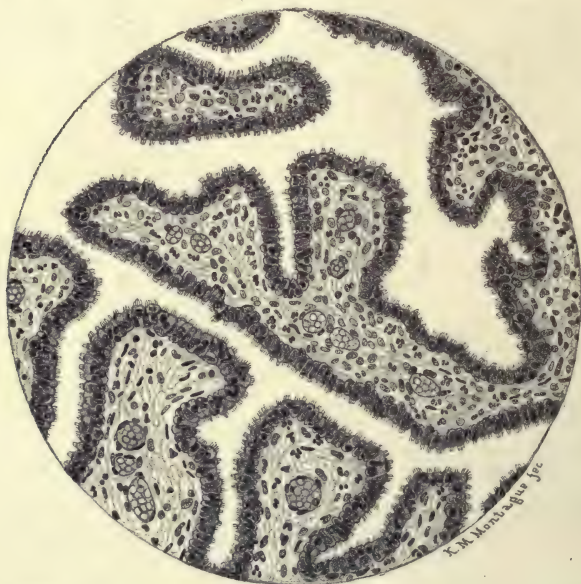


FIG. 335.—FROM A TRANSECTION OF THE AMPULLA OF THE OVIDUCT, SHOWING THE STRUCTURE OF THE MUCOSA. $\times 280$. (After Williams.)

type of connective tissue. Many of the connective tissue cells are of fusiform shape, and, unless specially stained or carefully examined, they closely resemble smooth muscle cells. The mucosa, however, contains no muscle except at the bases of the largest folds, into which occasional fibres from the adjacent muscular coat penetrate.

The muscular wall of the oviduct is formed by two layers of smooth muscle,—a broad inner circular layer, and an outer longitudinal coat, which is very unequally developed at different portions of the circumference, but is relatively thin in all parts, and is

entirely wanting at frequent intervals. The outer layer is usually broadest at the free margin of the oviduct and at its opposite side where the tube is attached to the broad ligament. The inner circular fibres are more or less obliquely disposed, and, toward the mucosa, the muscular bundles fuse insensibly with the cellular connective tissue of the mucous membrane.

The serous coat of the oviduct is continuous with the peritoneum. It consists of an outermost layer of endothelium which rests upon a subepithelial layer of connective tissue, by which it is firmly united to the muscular wall. This portion of the serous coat contains the larger vessels and nerves, which are distributed to the inner coats.

Blood Supply.—The arteries of the oviduct are derived from the uterine and ovarian vessels. The larger divisions find their way through the connective tissue of the serosa whence they send smaller branches inward to form a plexus between the layers of the muscular wall and among the bundles of circular muscle fibres. From this plexus capillaries are distributed to the muscular coat, and to the mucous membrane in which they form a rich subepithelial capillary plexus. The veins follow a similar course, and like the arteries, form an extensive plexus in the muscular coat. The abundance of vessels in the muscular wall of the oviduct has led to the description of this coat as the vascular layer of the organ.

The lymphatics arise by anastomosing plexuses in the mucosa, from which vessels pass to the serous coat and enter valved lymphatics by which the lymph is conveyed to the lymphatic nodes of the lumbar region.

The nerves are distributed from a plexus in the serous coat, to the muscular wall, and to the mucosa, in which they form a terminal subepithelial plexus.

THE UTERUS

The wall of the uterus consists of a mucous membrane, a muscular coat, and an outermost serous coat which is derived from the peritoneum and invests the body of the organ. The cervix uteri projects into the vaginal canal and the serous coat is there replaced by a reflection of the vaginal mucosa.

The serous coat of the uterus consists of endothelium which rests upon a thin subepithelial layer of connective tissue. It presents no peculiarities.

The muscular coat of the uterus consists of smooth muscle whose fibres are of large size (40 to 60 μ in length) and which are disposed in interlacing bundles. In the lower mammals these form quite regular layers—an outer longitudinal, a thick inner layer, most of whose fibres are circular, and an innermost, but less dis-

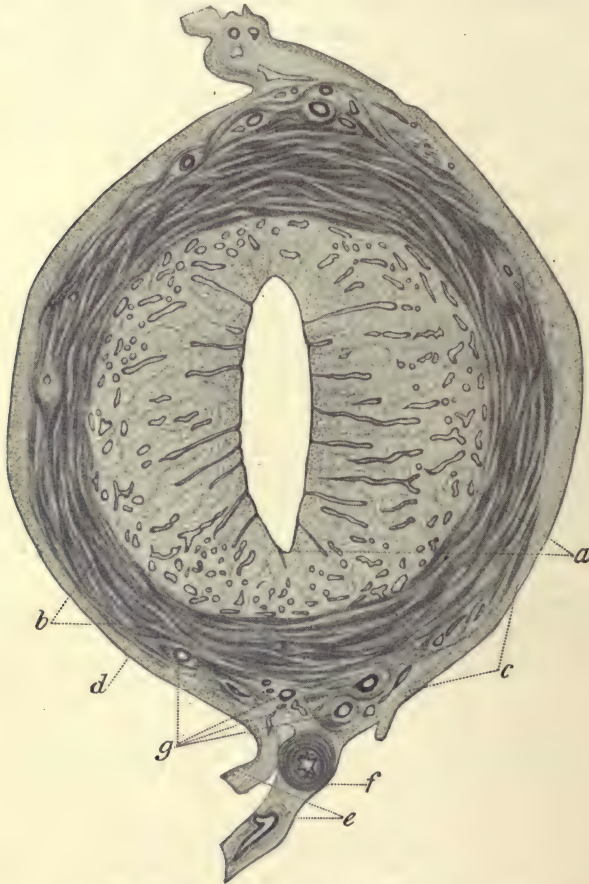


FIG. 336.—TRANSECTION OF THE UTERUS OF AN APE.

a, mucosa; *b*, circular muscle; *c*, longitudinal muscle; *d*, serous coat; *e*, lateral ligament; *f*, Wolffian tube; *g*, blood vessels. $\times 4$. (After Sobotta.)

tingent, submucous portion containing oblique and longitudinal fibres. The outer longitudinal and circular layers are separated by a fibro-muscular stratum containing a rich plexus of large blood vessels.

In the human uterus the arrangement of muscle fibres is much less regular, but follows a similar plan, though there is no distinct subdivision into layers. Nevertheless, careful examination reveals three indistinct strata which are intimately blended with one another. The outermost of these indistinct layers consists of irregularly disposed longitudinal fibres, the *stratum supravasculare*. This layer is in most parts very thin, and is best developed opposite the margin of the lateral ligament and in the cervix uteri. Within this is a broad layer of interlacing bundles of more or less circular fibres, which, from the slight obliquity of their course, frequently cross each other at acute angles. Intermingled with these circular bundles are many large blood vessels,

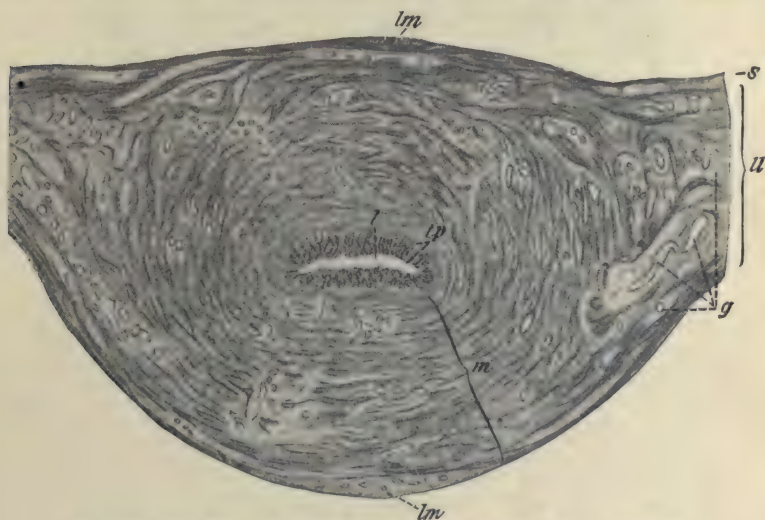


FIG. 337.—TRANSECTION THROUGH THE BODY OF THE HUMAN UTERUS.

g, blood vessels; *l*, lumen; *u*, broad ligament; *lm*, longitudinal muscle; *m*, circular muscle (the fibres are mostly oblique); *s*, serous coat; *tp*, mucosa. Hematoxylin and eosin. $\times 2$. (After Sobotta.)

from which both the mucous and muscular coats are supplied. This broad middle layer is therefore known as the *stratum vasculare*. The inner portion of this second layer passes insensibly into a thin innermost *stratum submucosum*, which again contains many longitudinal fibres, and upon which the mucosa directly rests.

The **uterine mucosa** is of considerable thickness (1 to 3 mm.). It is clothed with epithelium, and its tunica propria contains numerous tubular glands.

The epithelium is of the ciliated columnar type, and consists of a single row of cells. Apparently not all of its cells are provided with cilia, areas of ciliated, alternating with groups of non-ciliated epithelium. The epithelial layer is continuous with the epithelium of the uterine glands; in the region of the external os

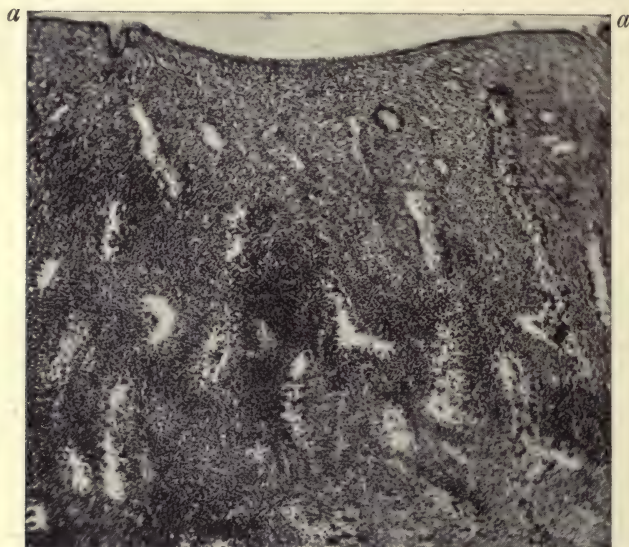


FIG. 338.—FROM THE UTERINE MUCOSA OF A GIRL OF SIXTEEN YEARS, SHOWING THE GLANDS OF THE BODY OF THE ORGAN.

a-a, lining epithelium. Hematein and eosin. Photo. $\times 115$.

uteri it is replaced by the stratified squamous epithelium of the vaginal mucosa. Ofttimes, and especially in multiparæ, the stratified squamous epithelium of the vagina is continued for some little distance within the canal of the cervix uteri; it never clothes more than the lower one-half to two-thirds of the cervical canal. The current resulting from the vibration of the intra-uterine cilia is directed toward the vagina (Hofmeier,* Mandl†).

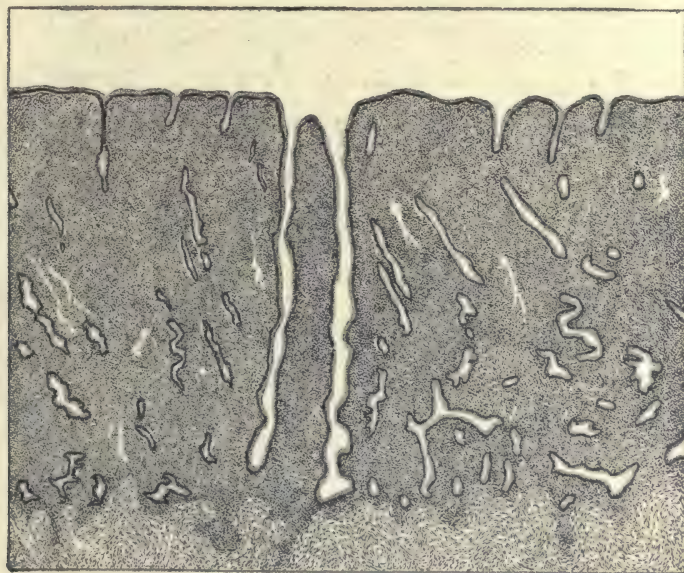
The *tunica propria* of the mucosa consists of a peculiar embryonal type of connective tissue, similar to that of the oviducts, which contains very few white and no elastic fibres, but which is richly supplied, in fact is literally packed, with cellular elements. These cells are ovoid or fusiform in shape, and many of them are branched; their nuclei, also, are ovoid and somewhat vesicular.

* Centralbl. f. Gynäkol, 1893.

† *Ibid.*, 1898.

Many leucocytes are found in the tunica propria, but these mostly occur in the vicinity of the lymphatics and smaller blood vessels with which the uterine mucosa is abundantly supplied. In the mucosa of the cervix uteri the development of the connective tissue appears to be more advanced, the cellular elements being relatively fewer; it also contains many fine fibres which appear to form a delicate network. At the external os uteri the tunica propria is continuous with the similar, though still more fibrous, layer of the vaginal mucosa.

The *uterine glands* are divisible into two types—those of the body of the organ, and those of its cervix. The former are, perhaps, to be regarded as tubular invaginations of the lining epithe-



K. M. MacLague, fec.

FIG. 339.—FROM A TRANSECTION OF THE UTERINE MUCOSA.

× 16. (After Williams.)

lium, whose function is one of epithelial regeneration rather than of glandular secretion. The tubules of the cervix uteri are true mucus secreting glands.

The uterine glands proper, those of the body of the organ, are slightly branched or forked tubules which traverse the entire breadth of the mucosa, presenting a characteristic spiral or corkscrew course; their blind extremities are often bent or turned to

one side, apparently from the proximity of the adjacent muscular coat. The glandular epithelium is of the columnar type and, like that of the free surface, is frequently provided with cilia, especially near the mouth of the gland. The epithelium rests directly upon the connective tissue of the tunica propria.

The cervical glands (*glandulæ uterinæ cervicales*) resemble those of the body of the organ in their tubular form and the columnar shape of their epithelium, but here the resemblance

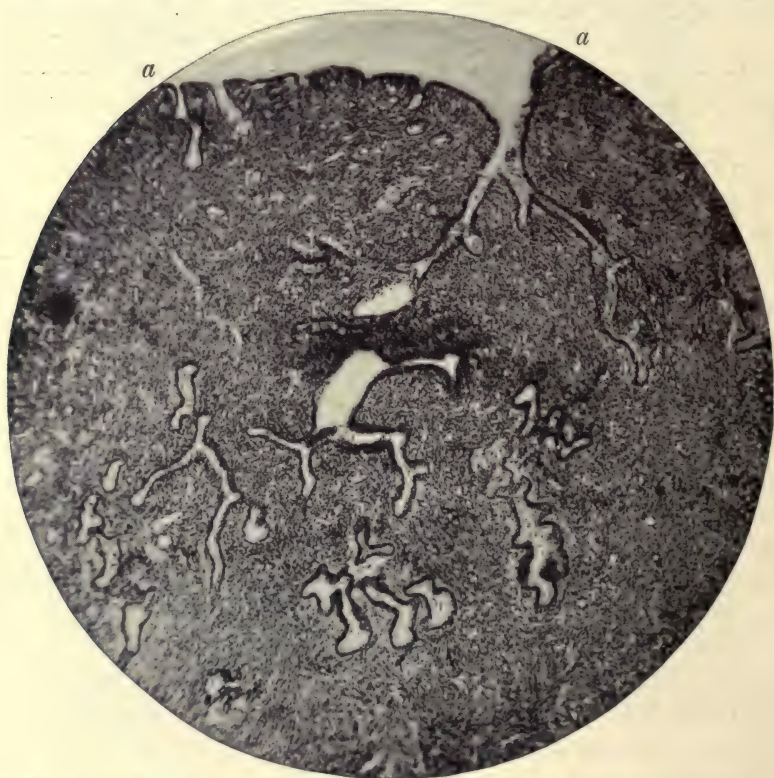


FIG. 340.—FROM THE CERVIX UTERI OF A GIRL OF SIXTEEN YEARS, SHOWING THE CERVICAL GLANDS IN SECTION.

a-a, lining epithelium. Hematein and eosin. Photo. $\times 102$.

ceases. The cervical glands are much branched, and their tubules present frequent dilatations, some of which, apparently from occlusion of their outlet, attain a macroscopic size, and are then known as *Nabothian follicles* (*ovula Nabothi*); they are filled with a tenacious mucous secretion. The glandular epithelium near

the crypt-like ducts is usually ciliated, like that of the surface, but in the secreting portions it consists of tall, clear, columnar cells which are in various stages of secretory activity, their product being a viscid glairy mucus, strings and granules of which are found within the lumen of the glands, as well as within the canal of the cervix uteri.

The uterine cavity is a relative term. In the virgin, the mucosa is considerably folded and its surfaces are almost in apposition, being only separated by a very limited amount of desquamated epithelium and cellular *débris*, to which, in the canal of the cervix uteri, the mucous secretion is added. During pregnancy, the development of the fetus within the uterine cavity distends its walls and so dilates the canal that it at last forms a sac of sufficient size to contain the fetus, which floats within the amniotic fluid inclosed by its membranes.

The blood vessels of the uterus enter through the folds of the lateral ligament and find their way, through the subepithelial connective tissue of the serous coat and the muscular wall, to all portions of the organ. In the vascular layer of the muscular coat they form an extensive plexus from which branches are distributed to the musculature and to the mucosa, the branches to the latter penetrating nearly to the surface, where they form rich, subepithelial, capillary and venous plexuses. The uterine arteries, like those of the ovary, possess a peculiar, spirally tortuous course. The veins accompany the arteries, but are less tortuous.

The lymphatics of the uterus arise by anastomosing channels in the mucous and muscular coats. They form a vascular plexus



FIG. 341.—A GLAND OF THE HUMAN CERVIX UTERI IN LONGITUDINAL SECTION.

× 90. (After Williams.)

in the serous coat and lead outward, through the lateral ligaments and pelvic connective tissue, to the lower lymphatic nodes of the lumbar region.

The nerves of the uterus are very numerous. They enter the serous coat from the ganglionic pelvic plexus, and are distributed to the vascular layer of the muscular coat. They there form a rich plexus, from which fibres are distributed to the musculature and to the walls of the blood vessels.

The distribution of nerves within the mucosa has not yet been thoroughly worked out. According to von Gawronsky* and Köstlin† nerve fibrils penetrate nearly to the surface and form a scanty subepithelial plexus, whence are derived fibrils which terminate between the epithelial cells.

THE MENSTRUATING UTERUS

The appearance of the phenomena of menstruation is accompanied by decided alterations in the structure of the uterine

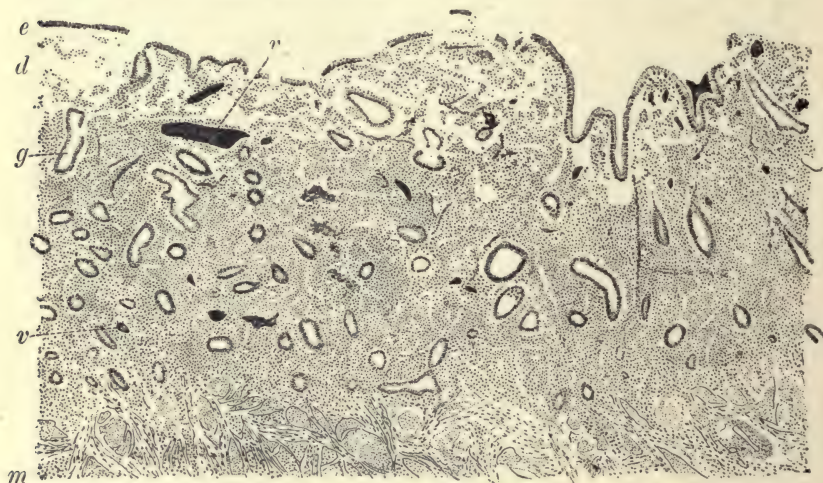


FIG. 342.—FROM A SECTION OF THE HUMAN UTERINE MUCOSA AT THE FIRST DAY OF MENSTRUATION.

e, epithelium; d, disintegrating layer; g, gland; v, blood vessel; m, muscular coat.
× 44. (After Minot.)

mucosa. In spite of the difficulty of obtaining sufficiently fresh and well preserved material, certain changes which characterize the menstruating uterus are now definitely known. These chiefly

* Arch. f. Gynäkol., 1894.

† Fortschr. d. Med., 1894.

consist in increased vascularity, hypertrophy of the elementary tissues of the mucosa, epithelial desquamation, and rupture of the blood vessels, with consequent hemorrhages. These changes are followed by a process of regression and later of regeneration, by which the uterine mucosa rapidly returns to its former condition.

The first or hypertrophic stage involves the epithelium, whose cells are elongated, and the tunica propria, in which many of the connective tissue cells undergo multiplication and enlargement. Thus the mucous membrane becomes greatly thickened; its glands, also, are increased in both length and breadth, becoming at the same time even more tortuous than before. The glandular hypertrophy involves both the uterine and the cervical glands; the secretion of the latter is much increased.

At the same time, the blood vessels become widely dilated, especially those near the surface, and broad thin-walled sinuses are formed beneath the epithelium. Finally these vessels rupture and hemorrhages occur into the substance of the mucosa as well as into the cavity of the organ; desquamation and disintegration of the superficial portions of the mucosa result. The menses which are thus formed contain blood, epithelium, connective tissue cells, and many leucocytes, which wander out from the blood vessels of the mucosa in large numbers. The greatly thickened and hemorrhagic mucosa is known as the *decidua menstrualis*.

Regression and regeneration follow rapidly upon one another, the mucosa gradually regaining its former condition. During this process fat droplets appear in many of the connective tissue cells. The epithelium is rapidly regenerated, the new cells arising from the epithelial remnants at the mouths of the uterine glands. In the course of a few days the mucosa regains its former quiescent condition.

THE GRAVID UTERUS

In the event of conception the uterine changes are even more pronounced than during menstruation. These alterations include the same processes of hypertrophy and thickening as occur in the decidua menstrualis; they involve the musculature as well as the mucosa but are not followed by regressive changes,—hemorrhage, desquamation, etc.—until parturition occurs.

The muscular wall undergoes an enormous increase both in the number and size of its fibres. The relatively short (30 to 60 μ) smooth muscle fibres of the uterine wall gradually increase in size to as much as eleven times their former length and two to

five times their breadth (Kölliker*). The connective tissue of the muscular coat also increases in volume and becomes more distinctly fibrous. After parturition, fat droplets appear within the muscle cells, and the muscular wall by gradual atrophy returns to its former condition.

In the mucosa the formation of a decidual membrane goes forward in a manner similar to the development of the decidua menstrualis, but the process is exaggerated. The tunica propria soon becomes divisible into two distinct, though not sharply defined, layers, a deeper *cavernous portion* which is permeated by broad vascular channels together with the atrophied remains of the uterine glands, and a superficial *compact layer* in which the vascular channels, except for the thin-walled venous spaces, are smaller and the connective tissue cells more closely packed.

Many of the connective tissue cells attain a large size and their nuclei are frequently multiple, or they may acquire an irregular polymorphonuclear form. Giant cells are thus produced in the compact layer of the mucosa of the gravid uterus; they are highly characteristic of this tissue and are known as *decidual cells*. Though it is frequently asserted that similar cells occur in the decidua menstrualis, this is denied by Minot,† who states that in a considerable number of menstrual decidua examined, no such cells were ever found.

The superficial epithelium is soon desquamated and the tunica propria comes into contact with the fetal chorion. The glandular epithelium is also partially degenerated, often becoming flattened and of irregular shape. It is frequently desquamated into the glandular lumen; this lumen is thus reduced to a narrow crevice, which is so elongated during the dilatation of the uterine wall that the axis of the glandular remnant becomes nearly parallel to the surface of the decidua.

The decidual membrane which is thus formed is divisible into three portions, according to its relation to the tissues of the embryo: 1, that portion upon which the developing ovum directly rests, which is known as the *decidua serotina* or *decidua basalis* but later forms the *placenta uterina* or maternal portion of the placenta; 2, at the margins of the implanted ovum the decidual tissues grow up around the ovum which is thus surrounded by the so-called *decidua reflexa* or *decidua capsularis*, which, after

* Handbuch, iii, 574.

† Laboratory Text-book of Embryology, 1903.

the early months of pregnancy, is gradually obliterated by the increasing growth of the fetus, and is finally replaced, its functions being progressively usurped by the newly formed placental tissues; 3, all the remaining portions of the decidual mucosa, those which line the greater part of the uterine cavity, collectively form the *decidua vera*, with whose surface, in the later months of pregnancy, the fetal chorion is intimate in relation.

The mucosa of the cervix uteri meanwhile becomes greatly hypertrophied and its glands much enlarged. This portion of the uterine mucosa does not, however, enter into the formation of the decidua vera; the changes occurring in its tissues, though similar, are much less pronounced.

THE PLACENTA

The human placenta at full term is formed partly by fetal and partly by maternal tissues, the former of which may be said to be implanted in the superficial layers of the latter. Hence on the fetal side the organ is limited by the fetal membranes, amnion



FIG. 343.—DIAGRAM SHOWING THE STRUCTURE OF THE HUMAN PLACENTA AS SEEN IN TRANSECTION.

The fetal blood vessels and maternal arteries are black; the maternal veins and intervillous blood spaces are white. *a*, amnion; *b*, chorion; *c*, chorionic villi; *d*, decidua; *e*, glandular layer of the uterine mucosa; *f*, muscular wall of the uterus.

and chorion, on the maternal side by the tissues of the decidua serotina, while between these boundaries is a broad interval which is occupied by a forest of arborizing processes of the fetal chorion, some of which, the *main stems*, completely span the interval, their tips being firmly embedded in the surface of the decidua, while others, the *free branches* or *floating villi*, pass from the lateral surfaces of the main stems and repeatedly subdivide, the tips of their branches floating free in maternal blood spaces which are therefore known as *intervillous spaces*.

Where the fetal chorion and maternal decidua are in direct contact at the margin of the placenta, the decidual cells extend inward to meet the opposed surface of the chorion, upon which they then expand to form the so-called *decidua subchorialis* (Fig. 349, page 432).

THE AMNION.—This is a thin membrane, of fetal origin, consisting of an epithelial coat and a thin layer of mesenchymal connective tissue. Its epithelium, whose surface is directed toward the fetus, consists of cuboidal or flattened epithelial cells which are derived from the ectoderm; they are firmly united with one another by means of intercellular bridges (Minot*). The connective tissue forms a thin transparent layer of embryonic tissue in which are many cells. From the inner surface of this layer delicate processes pass to the surface of the chorion, to which membrane the amnion is loosely attached.

THE CHORION.—This tissue includes a *membranous portion* which is in relation with the amnion, and a *villous portion* which forms the forest of placental villi already described as lying between the fetal membranes, on the one hand, and the maternal decidua on the other. That portion of the chorion which enters into the formation of the placenta is known as the *chorion frondosum*, in contradistinction to the remaining portion of the chorionic membrane which is loosely attached to the decidua vera and is called the *chorion laeve*.

The membranous portion of the chorion may be said to consist of two layers,—an inner or fetal layer of embryonic connective tissue, which is continuous with the similar tissue of the amnion and serves for the transmission of the fetal blood vessels on their way from the umbilical cord to the placental villi, and an outer layer which consists of intermingled groups of large cells, collect-

* *Loc. cit.*

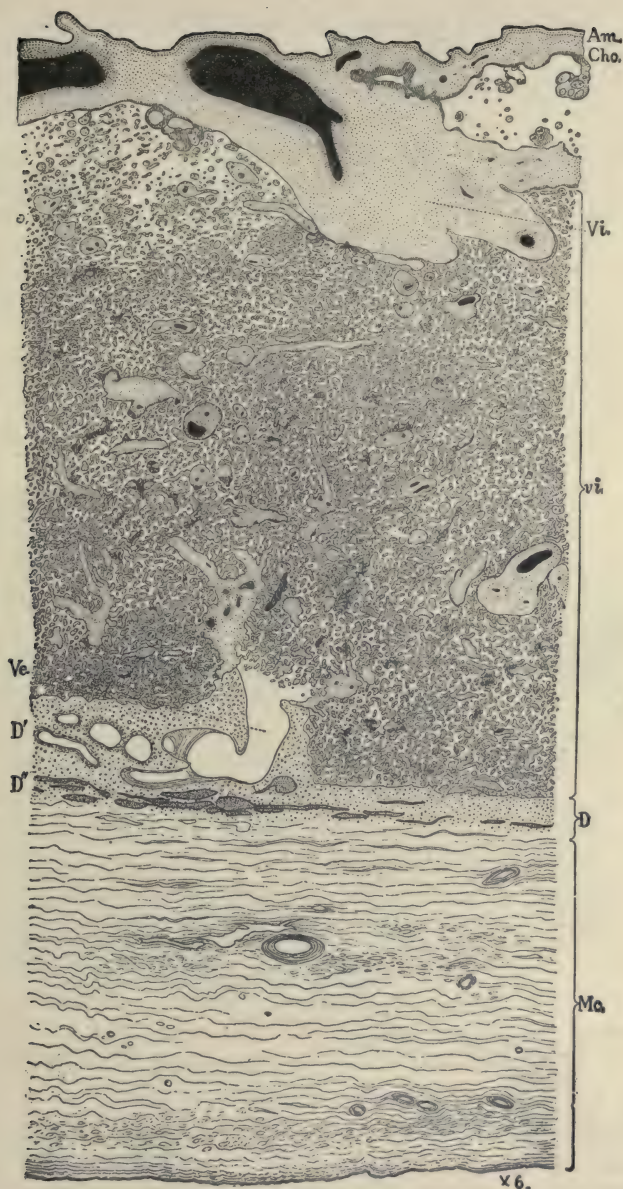


FIG. 344.—TRANSECTION OF THE WALL OF THE HUMAN UTERUS AT THE SEVENTH MONTH OF PREGNANCY, WITH THE PLACENTA IN SITU.

Am, amnion; *Cho*, chorion; *Va*, main stem of a chorionic villus; *vi*, villi in section; *D*, *D'*, decidua serotina; *Mc*, muscular wall of the uterus; *Ve*, uterine artery. The fetal vessels are black, the maternal white. The glandular remnants in the decidua are dark. $\times 6$. (After Minot.)

ively forming the *trophoblast*, together with masses of *canalized fibrin*.

The **trophoblast** consists of large ovoid cells. It presents a homogeneous appearance, not unlike that of the maternal decidua serotina, and is derived from the fetal ectoderm. Its cells form



FIG. 345.—HUMAN PLACENTAL TISSUES (AMNION AND CHORION) AT THE FIFTH MONTH. *Ep*, epithelium of the amnion; *Am*, amnion; *c*, cellular layer of the chorion; *Fib*, fibrillar layer; *Fbr*, canalized fibrin; *Str*, stroma; *Vi*, chorionic villi. $\times 71$. (After Minot.)

the larger part of the outer portion of the membranous chorion and are continued into the main stems of the chorionic villi. In the early months of pregnancy they occur in all the primitive villi of the placenta, where they are found on the surface of the connective tissue core, beneath the syncytium, and are known as the *cells of Langerhans*. Later they appear to degenerate, and are of less frequent occurrence in the chorionic villi.

The **canalized fibrin** is of doubtful origin. It forms irregular plate-like masses which either invade the substance of the membranous chorion or here and there clothe the placental surface of the mass of trophoblastic cells. Occasionally, and especially upon the surface of the chorionic villi, it apparently replaces portions of the syncytial membrane which elsewhere covers the villi, lines the maternal surface of the membranous chorion, and therefore forms the proper wall of the intervillous or maternal blood spaces.

Canalized fibrin consists of a granular eosinophilic mass which is pierced by many narrow clefts, hence the name.

The Chorionic Villi.—These innumerable processes form the greater portion of the placental tissues. They vary in size from the broad main stems to the very slender terminal branches of the floating villi. In the early condition of the placenta (fourth or fifth month of pregnancy) the villi are clothed with a double epithelial layer, of which the superficial takes the form of a syn-

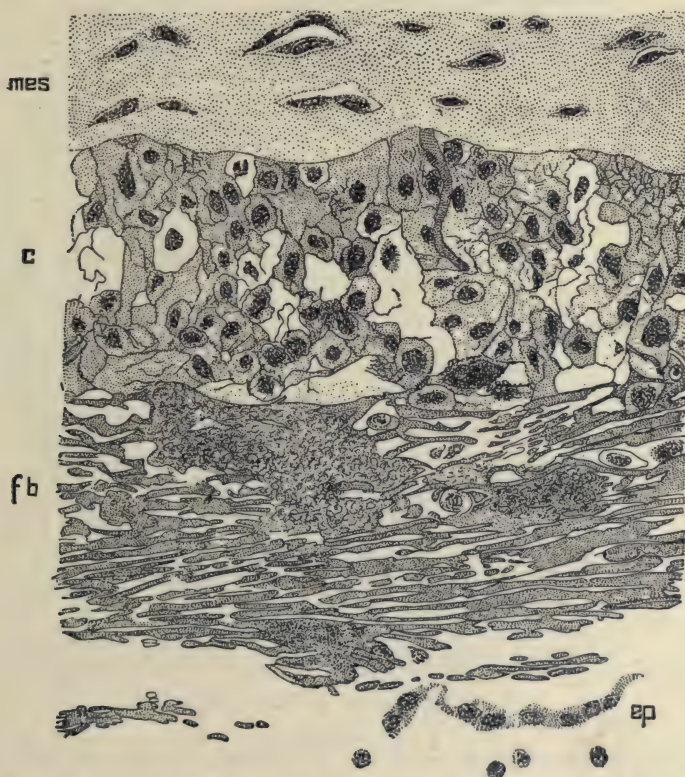


FIG. 346.—THE CHORION OF THE HUMAN PLACENTA AT THE SEVENTH MONTH.

c, cellular layer; *ep*, remnants of the epithelial layer; *fb*, canalized fibrin; *mes*, mesodermal stroma. $\times 445$. (After Minot.)

cytium, derived, according to Keibel,* from the endothelium of the maternal blood vessels; the deeper consists of a cellular layer, the cells of Langerhans. At later periods (seventh month to full

* Anat. Anz., 1889.

term) the syncytium is found to have undergone a peculiar alteration, having become much thinner, and having even completely disappeared from considerable portions of the villi, it being replaced by canalized fibrin; at other points the syncytial cyto-

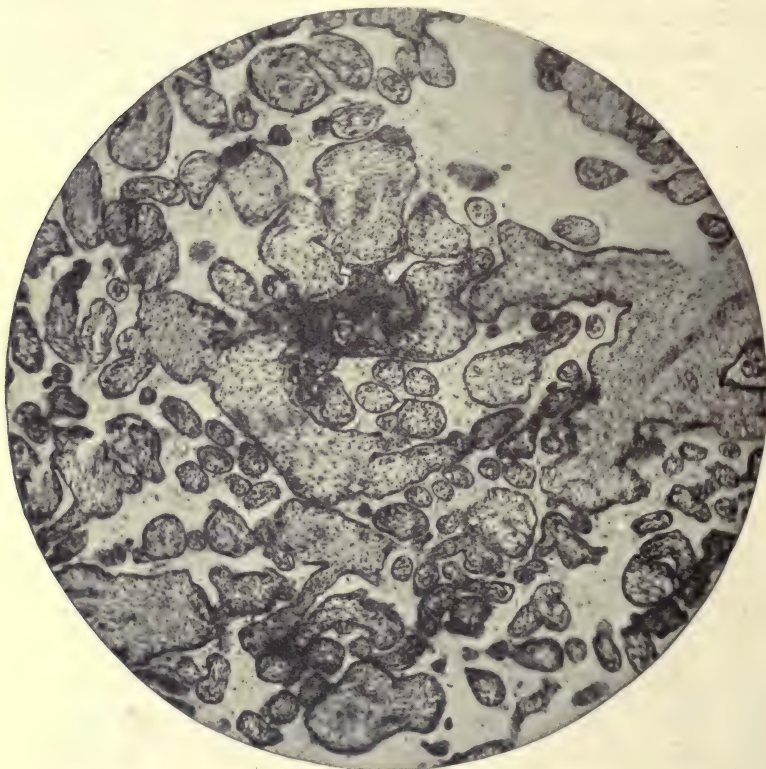


FIG. 347.—CHORIONIC VILLI FROM THE HUMAN PLACENTA AT FULL TERM.

Hematein and eosin. Photo. $\times 114$.

plasm is much thickened and the nuclei appear to be bunched or grouped within the thickened portions; these areas are known as *cell-knots* or *proliferation islands*. Here and there the degenerated cell-knots have been replaced by canalized fibrin. Wherever the main stems are inserted into the decidua the epithelium which formerly covered their tips appears to have also degenerated into a peculiar hyaline border zone.

Within its syncytium the substance of the villus consists of the superficial cells of Langerhans with their large ovoid nuclei, and a

core of connective tissue of a delicate embryonic type, in which are the *fetal* blood vessels. Even the smallest villi contain capillary loops of broad calibre, which are supplied by fetal arteries, derived from the umbilical arteries, which distribute their branches throughout the chorionic connective tissue. The fetal veins accompany the arteries.

THE DECIDUA SEROTINA (*Decidua Basalis*).—This portion of the maternal decidua receives the insertion of the chorionic villi; its superficial compact portion belongs rather to the placenta than to the uterine mucosa, since it separates from the uterine wall along with the chorionic tissues when the placenta is dislodged at parturition. The substance of this layer is formed by

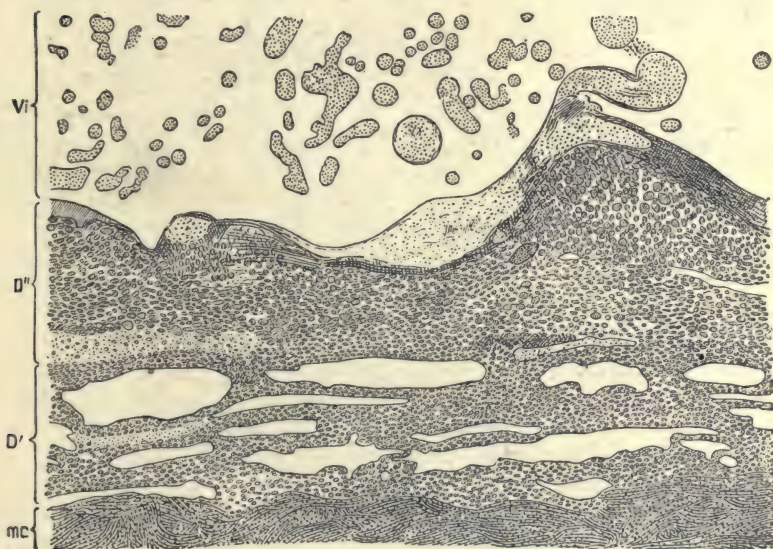


FIG. 348.—THE HUMAN DECIDUA SEROTINA AT THE SEVENTH MONTH.

D', cavernous layer of the decidua; *D''*, compact layer; *mc*, margin of the muscular coat of the uterus; *Vi*, chorionic villi, the spaces between which were filled with maternal blood. (After Minot.)

the decidual connective tissue in which the enlarged decidual cells are specially numerous. It transmits the maternal blood vessels, and with its surface the main stems of the chorionic villi, at their occasional points of attachment, are intimately blended. Here and there the decidual connective tissue is continued inward for some distance between the chorionic villi to form incomplete septa

which mark off the outer surface of the detached placenta into macroscopical areas or lobules, the placental *cotyledons*.

The distribution of the blood vessels of this part is specially interesting. The arteries enter from the muscular coat of the uterus and follow a spirally tortuous course through the decidua, until they arrive near the surface of the compact layer. Here their lumen suddenly broadens and their walls become relatively

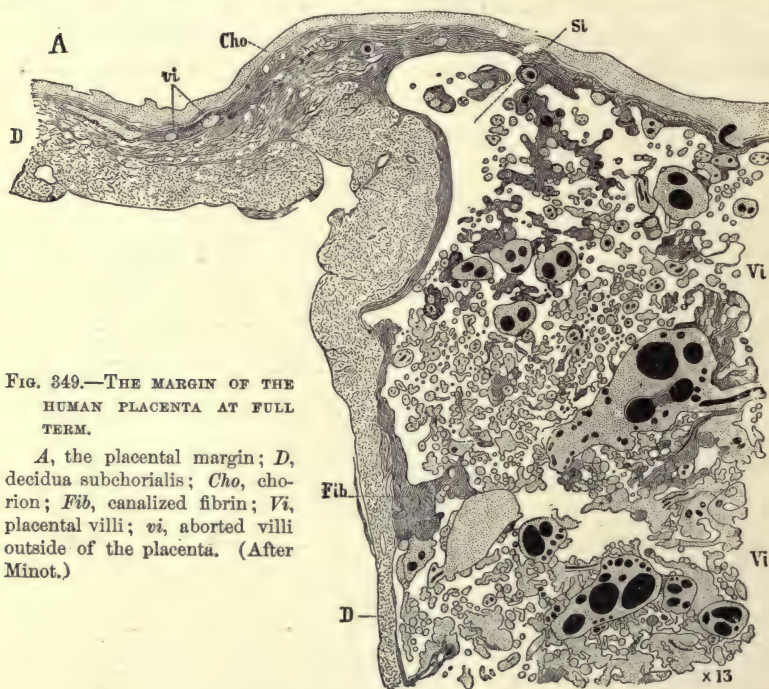


FIG. 349.—THE MARGIN OF THE HUMAN PLACENTA AT FULL TERM.

A, the placental margin; D, decidua subchorialis; Cho, chorion; Fib, canalized fibrin; Vi, placental villi; vi, aborted villi outside of the placenta. (After Minot.)

thin, consequently they are with difficulty distinguished from the veins. These arterial spaces at last turn suddenly and enter the placental tissues, pouring their contents directly into the lumen of the intervillous spaces; hence these are to be regarded as maternal blood spaces. The maternal veins also open directly from the intervillous spaces and, though much less tortuous, they retrace the course of the arteries to the vascular layer of the uterine musculature. We may liken the intervillous spaces to an enormously dilated capillary space, a great lake, as it were, within which the chorionic villi are suspended and of which the many maternal arteries form the inlets and the corresponding veins of the decidua

serotina, the outlets. At the margin of the placenta the border of this great intervillous lake is relatively free from villi and forms the so-called *circular sinus*, a space which is obviously not a true sinus, in that, not having a proper wall, it can not be said to possess definite boundaries.

Since the fetal blood vessels of the placenta are everywhere contained within the connective tissue of the chorionic villi, while the maternal blood circulates only in the intervillous spaces, it is obvious that there can be no direct communication between the fetal and the maternal blood channels, nor can there be any interchange whatsoever of fetal and maternal blood cells. The course of the fetal blood can be traced from the umbilical arteries to the arteries of the villi, thence through the blood capillaries to the venous radicals within the villi; these return the fetal blood, through veins in the connective tissue of the chorion, to the larger venous branches in the membranous chorion, which finally unite to form the umbilical vein.

THE UMBILICAL CORD

This organ transmits the two umbilical arteries which are spirally wound about the umbilical vein. These vessels are embedded in a non-vascular, gelatinous, connective tissue, known as the *jelly of Wharton*, which is rich in cells and ground substance. The fibres, as in all embryonic tissue, are poorly developed and form only a loose net of very delicate fibrils.

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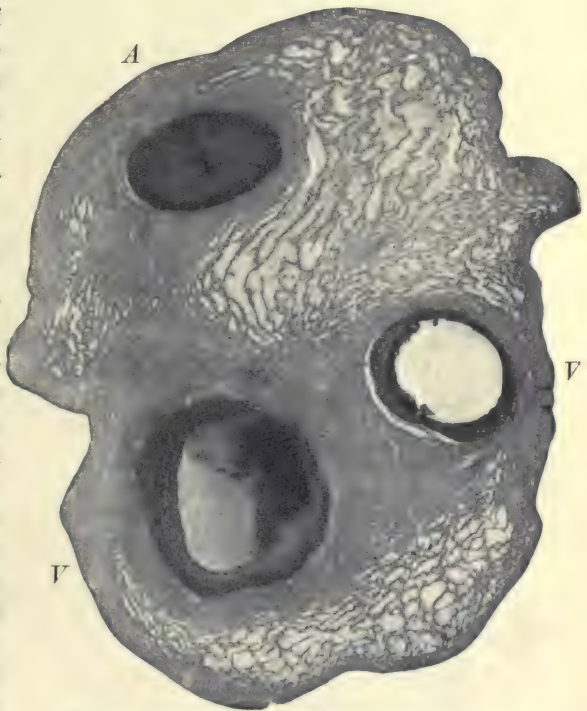


FIG. 350.—TRANSECTION OF THE UMBILICAL CORD OF A NEW-BORN HUMAN INFANT.

A, artery; V, V, veins. Hematein and eosin.
Photo. $\times 10$.

The connective tissue cells and fibres are frequently arranged in membranous bands which extend lengthwise of the cord and in transections present a peculiar concentric arrangement, the delicate membranes alternating with broad tissue spaces, and often inclosing the blood vessels or forming incomplete concentric lamellæ about the circumference of the cord. The surface of the cord is clothed with an ectodermal layer of flattened epithelium which occasionally forms several layers of cells.

The umbilical vessels, the veins as well as the arteries, are peculiar in that they possess unusually thick muscular walls. Their smooth muscle fibres are disposed both longitudinally and circularly. In transection the endothelial lining of the vessels is seen to be thrown into prominent folds by the contraction of the thick muscular wall.

Remnants of the allantois, and occasionally of the yolk sac as well, are found in the fetal end of the umbilical cord even at full term. These appear in the form of indistinct epithelial tubes or columns, whose cells often show evidences of degenerative changes.

THE VAGINA

The vagina is a fibro-muscular sheath whose wall is divisible into three coats—mucous, muscular, and serous.

The mucous membrane is clothed by a layer of stratified squamous epithelium, and is thrown into numerous folds or rugæ. The epithelium rests upon a fibrous basement membrane. The tunica propria is formed by a close-meshed areolar tissue which, in its deeper and looser portion, is permeated by vascular channels of considerable size. This deep vascular layer is frequently described as a submucosa; it rests directly upon the muscular wall. The surface of the mucosa presents numerous conical papillæ which project well into the epithelial layer.

The musculature of the vagina contains smooth or involuntary fibres, and is divisible into an inner circular and an outer longitudinal layer. The muscle fibres are long and slender. Considerable connective tissue is distributed among the muscle bundles. The latter are arranged in more or less parallel layers which are united by the delicate bands of connective tissue.

The outer fibrous coat consists of dense areolar tissue which is well supplied with elastic fibres. It loosely unites the vaginal wall to the surrounding tissues. In this coat is a plexus of blood-vessels and lymphatics, from which branches pass to the muscular

coat, and to the mucosa, in which they form an abundant plexus. An extensive nerve plexus, in which are many small ganglia, is



FIG. 351.—FROM A SECTION THROUGH THE WALL OF THE VAGINA OF A GIRL SIXTEEN YEARS OLD.

a, mucosa; *b*, muscular coat; *c*, fibrous coat, containing large thin-walled vascular spaces. Hematein and eosin. Photo. $\times 47$.

also found in the fibrous coat; it distributes motor branches to the muscular wall and to the blood vessels, and sensory fibres to the mucosa, in which they end in relation with the cells of the lining epithelium.

The vaginal mucosa is reflected upon the outer wall of the cervix uteri, and at or near the external os it is continuous with the mucosa of the uterine cavity. Though occasional glands have been found in the vaginal mucous membrane, lined either by mucus secreting or by ciliated cells, these glands would seem to be properly considered as anomalies, since they are usually absent, the mucoid secretions of the vaginal canal being chiefly provided by the abundant supply of mucus from the cervical glands of the uterus. The vaginal mucosa is continuous below with that of the vestibule.

THE EXTERNAL GENITALS

The vestibule is supplied with a mucosa which offers a gradual transition from the vagina, on the one hand, to the skin on the other. Its stratified squamous epithelium becomes in this way

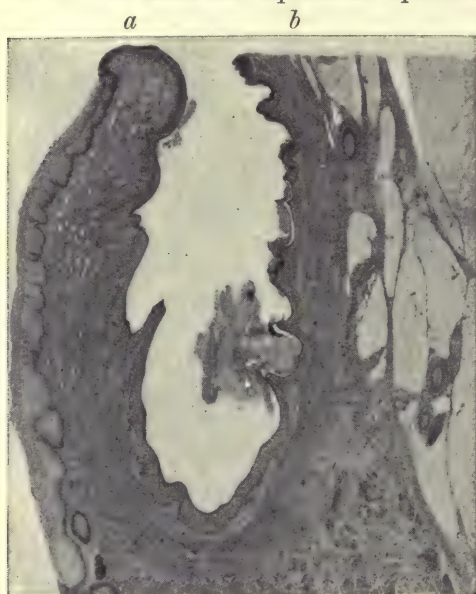


FIG. 352.—TRANSECTION OF A LABIUM MINUS OF AN INFANT.

a, labium minus; *b*, border of the labium majus; *c*, adipose tissue of the latter. Hematein and eosin. Photo. $\times 12$.

gradually more and more like that of the skin, eleidin granules first, and keratin later appearing on the outer surface of the labia minora. The epithelium of the labia majora is identical with that of the skin.

The labia minora are formed by a fold of the mucosa which is provided with exceptionally tall papillae. Small sebaceous glands open directly upon the surface of the stratified squamous epithelium. There are no hair follicles in relation with these glands, and the labia

minora contain no adipose tissue. They are richly supplied with blood vessels.

The **labia majora** are formed by similar folds whose inner surface resembles the adjacent portion of the labia minora, but whose outer surface is cutaneous and is supplied with sebaceous and sudoriparous glands and with numerous hair follicles. The sub-epithelial areolar tissue is very dense and its deeper portion contains much fat.

The **clitoris** consists of a mass of erectile tissue, homologous with the corpora cavernosa and glans penis of the male; it is covered by a fold of the mucosa. It is well supplied with nerves, which terminate in tactile corpuscles, end bulbs, and genital corpuscles. In this vicinity also, as well as in the region of the labia, Pacinian corpuscles are occasionally found.

The **hymen** is formed by a reduplication of the vestibular mucosa. Its inner surface is similar to that of the labia minora and vagina; its outer is like that of the cutaneous surface, except that it contains no hair follicles.

The **glandulæ vestibulares minores** are a group of small mucus secreting glands, similar in structure to the glands of Littre in the male, which occur in the vestibular mucosa in the vicinity of the meatus urethræ.

The **glandulæ vestibulares majores** (*glands of Bartholin*) form a paired tubulo-alveolar mucus secreting gland which opens by a narrow duct into the groove between the hymen and labium minus. The tubular alveoli are lined by columnar mucus secreting cells; the ducts are clothed with columnar epithelium, which, as they approach their termination, becomes double-rowed, and finally changes to a stratified squamous epithelium similar to that of the surface upon which they open. These ducts frequently present saccular dilatations.

THE MAMMARY GLANDS

From a strictly histogenic standpoint the mammary glands should be considered as appendages of the skin, and as such should more properly have been considered in the chapter devoted to that subject. Yet these glands are so closely related to the reproductive functions, attaining their full development only in the lactating female, that it seems equally proper to consider them at this time as accessory reproductive organs.

Each mammary gland consists of fifteen to twenty-four (Kölle-

ker*) lobes, each of which is of itself a tubulo-acinar gland whose lactiferous duct opens on the surface of the nipple near its apex. The mouths of these ducts are narrow: their terminal portions in the deeper part of the mamilla are much broader, thus forming in each lobar duct a sort of terminal saccule or *lactiferous sinus*. The main lactiferous ducts subdivide in an arborescent manner into many interlobular ducts, about which are clustered the groups of secreting alveoli, each group forming one of the many lobules included in a lobe of the gland. The structure of the lobule, as well as the general appearance of microscopical sections of the gland, varies much according to the stage of development and the condition of activity of the organ.

THE ACTIVE GLAND.—During lactation the glandular alveoli are so numerous as to form by far the most prominent portion of the gland. Each lobule consists of a cluster of saccular alveoli which open by short alveolar ducts into the interlobular ducts of the connective tissue which invests the lobules of the gland. The alveoli are closely packed within the lobule. In form, except for the regularity of their epithelium and the distinctness of their cell outlines, they might well be compared with the intralobular alveoli of the salivary glands. They possess, however, a broader lumen.

The actively secreting alveoli are lined by cuboidal or low columnar cells which vary much in height even within the same alveolus, and are often considerably flattened. Their secretory activity is indicated by the appearance of fat droplets, which accumulate within the distal portion of their cytoplasm. These droplets apparently push toward the free surface of the cell, gaining somewhat in size as well as in number, until they finally occupy the greater part of the distal end of the cell and are separated from each other by only a narrow interval of albuminous cytoplasm. At last they are discharged into the broad lumen of the alveolus, where they apparently still retain a thin albuminous envelope which prevents their cohesion and consequent fusion, and thus permits their suspension in the albuminous, fluid portion of the milk.

The spheroidal nuclei of the secreting cells during this process are crowded to the base of the cell, and after the discharge of the secretion the shrunken but nucleated cell remnants remain *in situ*; after a period of rest, the cells apparently resume their secretory function. It appears probable that each cell in its life

* Handbuch, iii, 590.

history may repeatedly pass through the cycle of secretory changes, though the exact number of such cycles which an individual cell may present obviously does not admit of demonstration.

As a rule, the active epithelium consists of a single row of cells, though here and there they appear as if piled upon one another

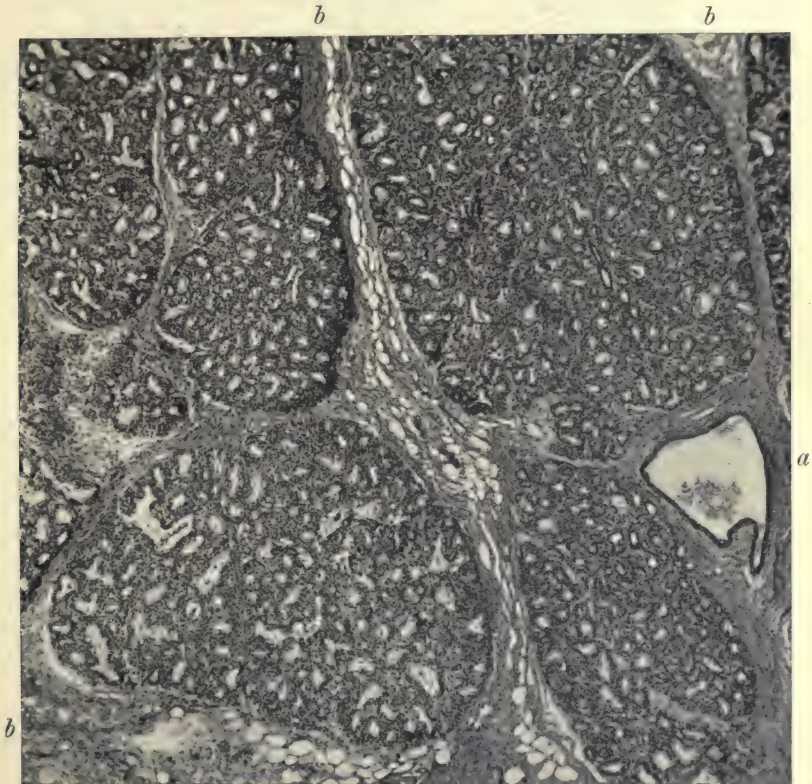


FIG. 353.—FROM THE ACTIVELY SECRETING MAMMARY GLAND OF A WOMAN.

Several lobules are included. *a*, interlobular duct; *b*, interlobular connective tissue.

Hematein and eosin. Photo. $\times 52$.

to form a double layer. The epithelium rests upon a reticular or homogeneous basement membrane, within which are occasional *basket cells* (*Korbzellen*). The alveoli of the active gland are so closely packed that a connective tissue tunica propria is no more than scarcely demonstrable. The thin tunica propria is, however, richly supplied with blood capillaries, lymphatic vessels, and nerve fibres.

The ducts of the mammary gland are lined by either a single or double row of low columnar cells. They possess a relatively broad lumen. Their membrana propria is supported by a thin



FIG. 354.—MODEL OF A RECONSTRUCTION OF AN INTRALOBULAR DUCT AND ITS ACINI FROM THE ACTIVE MAMMARY GLAND OF A WOMAN.
× 200. (After Maziański.)

connective tissue wall, containing both circular and longitudinal elastic fibres but no muscle (Kölliker,* Schäfer†). The elastic fibres of the smaller ducts are poorly developed, but in suitable specimens the longitudinal fibres are readily seen even in very small branches. Beyond the lactiferous sinus the duct epithelium changes to a stratified squamous variety which is continuous with that of the cutaneous surface of the nipple.

The glandular lobules are firmly united by strong septa derived from the dense areolar tissue in which they are embedded. In the deeper parts of the gland occasional lobules of fat are found in this tissue. Within the nipple and beneath the adjacent portions of the areola, smooth muscle fibres are also found. These are arranged in circular bundles at the base of the nipple, with longitudinal fibres within its substance which, at the base of the mammilla, diverge in radiating bundles into the subcutaneous tissue of the areolar zone. Contraction of these fibres elevates and hardens the nipple, thus stimulating the action of the erectile tissues.

Embedded in the subcutaneous tissue of the areola are also a number of small accessory lactiferous glands known as the *Glands of Montgomery* (*Areolar Glands of Duval*).

THE RESTING GLAND.—With the cessation of lactation the glandular alveoli undergo a rapid atrophy, and are replaced by connective tissue derived from the interlobular stroma. The ducts contract and the epithelium piles up to form a two-rowed, or even thicker, layer. The alveoli are reduced to mere buds from the terminal ducts, and their lumen is almost obliterated; their epithelium is similarly massed into a double layer of small cells. The lobules are reduced in size and consist only of a few

* Handbuch, iii, 591.

† Quain's Anat., iii, pt. iv.

shrunken alveoli clustered about the termination of an interlobular duct. The lumen of the alveoli, if any, contains no secretion, and that of the ducts; except for a little granular albuminous material and an occasional leucocyte, is empty.

The connective tissue stroma is much increased in volume, and in places shows a marked infiltration with fat. The alveolar tissue of the mammary gland at all times contains wandering leucocytes, and many granule cells, both acidophile and basophile in character.

With the appearance of pregnancy the gland promptly re-enters a state of activity; its alveoli multiply; its connective tissue becomes relatively diminished in volume; its lobules are reformed and their alveoli finally begin secretion, a process which is heralded by the formation of a granulo-fatty colostrum, a rather serous fluid in which are suspended large numbers of *colostrum corpuscles*, large spheroidal cells, resembling leucocytes in their general form and in the character of their nuclei, but which possess a broad rim of cytoplasm often containing numbers of fat globules of varying size. Their cytoplasm has also been shown to contain neutrophile granules of Ehrlich similar to those of the polynuclear leucocytes (Michaelis *).

The origin of the colostrum corpuscles is still somewhat in doubt, though modern technique has gradually discredited the theory of their origin from desquamated remnants of the alveolar epithelium, and shows them to be more probably enlarged leucocytes which have wandered through the alveolar wall and have

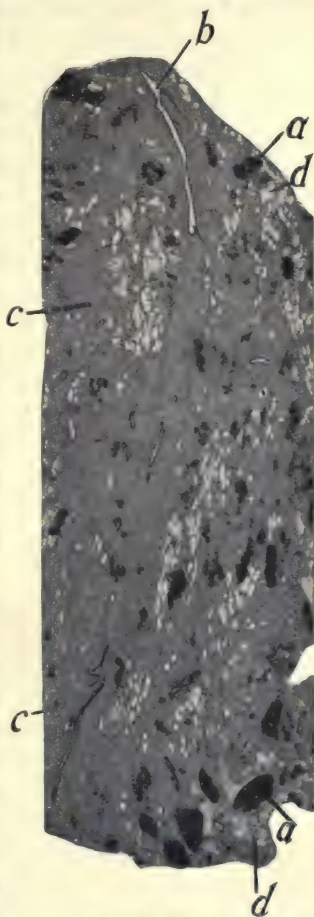


FIG. 355.—FROM A SECTION OF THE HUMAN MAMMARY GLAND IN THE RESTING CONDITION.

a, remnants of the glandular alveoli; b, duct; c, connective tissue; d, adipose tissue. Hematein and eosin. Photo. $\times 10$.

* Arch. f. mik. Anat., 1898.

thus found their way into the lumen, where they take on a phagocytic activity and continue their growth. The following facts may be mentioned in support of this theory : *a*, leucocytes can be readily found between the cells of the alveolar epithelium as well as in the lumina of the saccules ; *b*, the colostrum corpuscles examined in a fresh condition on a warmed slide have been repeatedly shown to possess the property of amoeboid motion ; *c*, the colostrum corpuscles, when stained, present the same granular and non-granular varieties as do the leucocytes of the blood ; *d*, finally, the colostrum corpuscles have been shown to undergo mitotic cell division (Bizzozero and Ottolenghi *), a phenomenon which we should hardly expect to find in degenerated and desquamated epithelial cell remnants.

The blood vessels of the mammary gland are specially abundant. They form rich capillary plexuses about the walls of the active alveoli. Many of the venules coming from these plexuses converge toward the areola, where they form an incomplete venous circle (*circulus venosus of Haller*) from which the efferent veins take their origin.

The lymphatics of the mammary gland are also numerous. They take origin from broad channels among the alveoli and enter a rich plexus about the interlobular ducts. From here several vessels pass to the lymphatic nodes of the axilla.

The nerves of the mammary gland are distributed to the vascular walls, to the smooth muscle of the areola and nipple, to the alveolar epithelium, and in the connective tissue of the nipple and areola they occasionally terminate in tactile and Pacinian corpuscles.

Among the secreting alveoli the nerve fibres form an epilemmal plexus beneath the *membrana propria*, from which fibrils penetrate between the epithelial cells, upon which they end in minute granular varicosities (Arnstein †).

MILK

Milk, secreted by the active mammary gland, consists of an emulsion, in which fat droplets, varying in size from $2\ \mu$ to $20\ \mu$ or more, are suspended in a watery albuminous fluid. Each fat droplet is presumably invested with a thin coat of casein, derived from the cytoplasm of the secreting epithelium. Occasionally leucocytes occur in the milk, but never in large numbers, and like the similar colostrum corpuscles, they are mostly confined to the earlier periods of lactation.

* *Ergeb. d. Anat. u. Entwickl.*, 1899.

† *Anat. Anz.*, 1895.

CHAPTER XXII

THE DUCTLESS GLANDS

UNDER this heading it will be convenient to consider the suprarenal, thyroid, parathyroid, carotid, and coccygeal glands, and the hypophysis cerebri.

I. THE SUPRARENAL GLANDS

The suprarenal glands (*adrenals*) are two glandular masses situated above but in close relation with the upper extremity of each kidney. On section the adrenal is seen to be readily divisible into a bright yellow or brownish-yellow cortex and a more vascular, and hence darker and somewhat reddish, medulla, whose central portion transmits several large veins which make their exit from an indentation in the anterior surface of the organ, known as the *hilum*.

The organ is inclosed by a connective tissue capsule of considerable thickness. From the inner surface of the capsule delicate fibrous trabeculae pass inward and subdivide the epithelial parenchyma of the organ into cell groups and columns, which vary in their appearance according to the distribution of the connective tissue trabeculae. The organ may be thus divided into a central *medulla* and a peripheral *cortex*. In the medulla the connective tissue presents an irregular areolar arrangement; the more regular, though varying form of the areolae in the cortex, subdivides this portion of the organ into three more or less distinct layers, which were first described by Arnold * as the *zona glomerulosa*, *zona fasciculata*, and *zona reticularis*.

In the *zona glomerulosa* the connective tissue trabeculae subdivide the epithelium into spheroidal groups of cells, many of which are continuous with the cell columns of the adjacent *zona fasciculata*. The glomerulate layer is relatively thin and lies close beneath the capsule.

* Arch. f. path. Anat., 1866.

The stroma of the zona fasciculata is continued inward from the glomerulosa, but is so drawn out as to form elongated areolæ, inclosing cell columns of considerable length, which are disposed

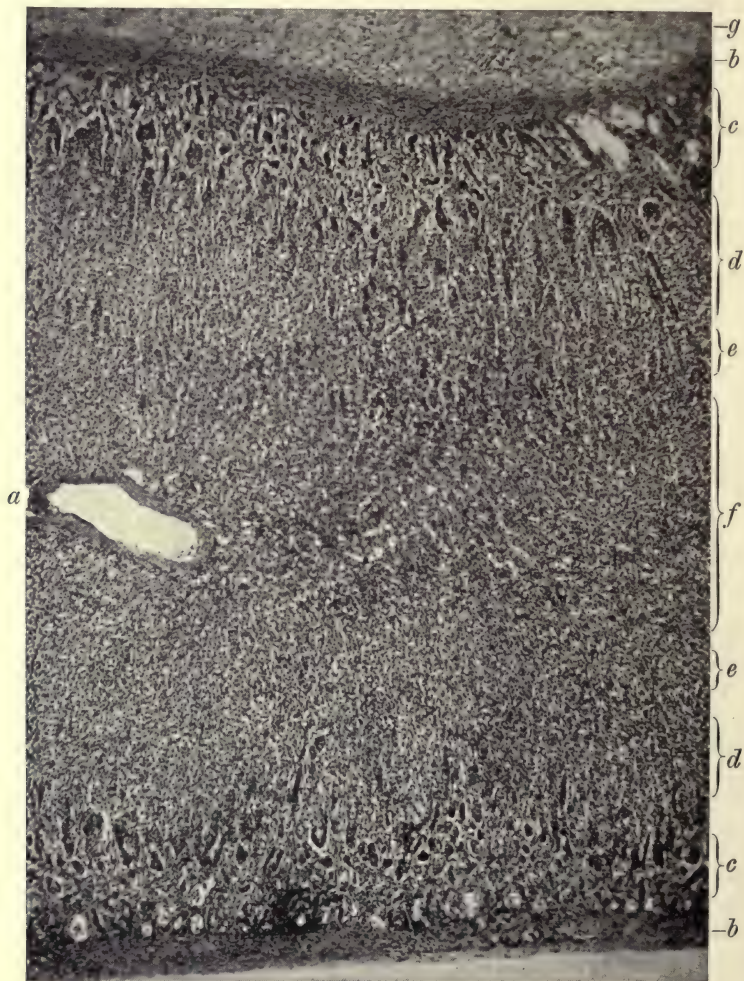


FIG. 356.—FROM A SECTION THROUGH THE HUMAN ADRENAL.

a, central vein; *b*, capsule; *c*, zona glomerulosa; *d*, zona fasciculata; *e*, zona reticularis; *f*, medulla; *g*, peri-adrenal adipose and areolar tissue. Hematein and eosin. Photo. $\times 45$.

in a radial manner. This is the broadest of the three cortical zones and is interposed between the glomerulosa and reticularis.

At the inner border of the zona fasciculata the connective tissue bundles pass insensibly from the regular columnar arrangement of this layer into a reticular maze. The resulting cell groups are of very irregular form and compose the innermost cortical layer, the zona reticularis. This layer is the thinnest and least distinct of the three zones of the cortex. It can often be more readily distinguished by the highly pigmented condition of its cells, than by the mere form of its cell columns. In man it passes almost insensibly into the medulla; in many animals—e. g., the dog, cat, and pig—there is a sharp demarcation between the zona reticularis and the medulla, produced by a thin membranous layer of connective tissue which apparently results from the fusion of the central ends of the fibrous bands in the cortical stroma. Such a membranous septum is usually wanting in the human adrenal.

The connective tissue stroma of the adrenal consists of a delicate vascular network, which in the cortex contains very few if any elastic fibres. Flint* has shown that this connective tissue is, in large part, at least, a reticular tissue. The capsule consists of dense bundles of white fibrous tissue among which are many elastic fibres. The stroma of the medulla is also richly supplied with elastic tissue.

The epithelium of the zona glomerulosa is arranged in spheroidal groups or in hooked or slightly coiled columns which are continuous with the straight columns of the fascicular zone. The cells of the zona glomerulosa are closely packed within the connective tissue meshes and the cell outlines are very indistinct. Wherever their outlines can be readily distinguished the cells are seen to be of columnar shape and are arranged in slender columns whose cells are often grouped about an indistinct central lumen. The cytoplasm of the cells of this zone is finely granular and stains readily with acid dyes. Occasional minute fat droplets appear in the innermost cells of the group, but these are never so abundant as in the more internal portions of the cortex. The nuclei in this zone are spheroidal in shape and rich in chromatin; they present frequent mitoses (Canalis †), but these are more abundant in early life than in the adult.

The cells of the zona fasciculata are highly characteristic. They are arranged in long straight columns which extend from the zona

* Contrib. to the Sc. of Med. ded. to W. H. Welch, 1900.

† Internat. Monatschr. f. Anat. u. Physiol., 1877.



FIG. 357.—FROM A TRANSECTION OF THE HUMAN ADRENAL.

The figure includes one half the breadth of the organ; it extends from the central veins in the middle of the medulla to the capsule on the free surface. *a*, peri-adrenal connective tissue; *b-b*, capsule; *c*, zona glomerulosa; *d*, zona fasciculata; *e*, zona reticularis; *f*, medulla; *g*, central vein in transection. Hematein and eosin. Photo. $\times 60$.

glomerulosa inward to the zona reticularis. The cells are columnar or polyhedral in shape; many of them contain minute fatty droplets in great abundance. This fat is readily blackened by osmic acid. Arnold,* by extraction with ether, obtained crystals of palmatin and stearin from the suprarenal gland. Plecnik,† however, considers that the adrenal fat differs in its ultimate chemical properties from the other fat of the body. Each columnar group consists of cells which are, as a rule, in approximately the same stage of fatty metamorphosis, and the cell columns of this zone may be divided into those which are distinctly acidophile and those which are distinctly fatty, though between these extremes there are many intermediate stages.

The acidophile cells are ovoid or polyhedral elements which possess one or two highly chromatic spheroidal nuclei and a finely granular cytoplasm. On careful examination with high magnification, extremely minute fat droplets may often be demonstrated even in the most characteristic of these cells; with lower magnification these are frequently invisible.

The fatty cells possess a spheroidal nucleus which is usually vesicular in character; occasionally it is highly chromatic. Frequently the apparent chromatolysis seems to progress in exact ratio to the accumulation of fat; those cells in which the fatty metamorphosis is more advanced present the more typically vesicular nucleus. With the progress of the fatty metamorphosis the cell outlines are again lost and the granular acidophile cytoplasm gradually replaced. The presence of fat in the broad zona fasciculata is partially responsible for the bright yellow color of the cortex of the organ.

The cells of the zona reticularis are similar to those of the zona fasciculata, though the fatty metamorphosis is less pronounced. In one particular, however, the cells of this layer are remarkable. They contain an abundance of a peculiar brownish-yellow pigment which occurs both in the form of coarse granules and as a diffuse coloration of the cytoplasm. The spherical nuclei, highly chromatic or only slightly vesicular in character, are not invaded by the pigmentation. The volume of pigment varies greatly in different individuals; it is usually absent in young persons, but is, as a rule, present after the twentieth year of life (Maass ‡).

The epithelial cells of the medulla are ovoid elements with one or two spherical nuclei, which in many cases possess a vesicular

* *Loc. cit.*

† Arch. f. mik. Anat., 1902.

‡ Arch. f. mik. Anat., 1889.

character; in other cells they consist of a dense, almost solid, mass of chromatin. The shape of the cell groups in the medulla varies greatly; usually they form small spheroidal masses or short columns. The cells are frequently arranged in a more or less tubular form but without a distinct lumen. Frequently they surround a minute capillary vessel. The medullary cells presumably pour their secretion into the blood vessels, whose broad capillaries or sinusoids (Minot*) permeate the delicate connective tissue bands which inclose the cell groups. Felicine† claims to have demonstrated the presence of minute intra- and intercellular secretory canaliculi which open directly or indirectly through broader *lacunæ*, into the blood vessels.

The cell groups of the medulla, like those of the cortex, are divisible into the acidophile and the fatty types; the former are the more abundant, but the fatty metamorphosis is scarcely ever so advanced as in the cortex. There is, however, great variation in the size of the medullary cells. The larger ovoid elements form the typical groups; between these groups are narrow cell columns consisting of much smaller and less highly acidophile cells, which are arranged in slender columns and scattered irregular masses.

In the vicinity of the central veins, small nerve trunks are found, and occasional minute ganglia or isolated nerve cells occur along their course. These are not to be confused with the large ovoid epithelial cells of the medulla.

BLOOD SUPPLY.—The arteries which supply the suprarenal glands form a *plexus* of vessels in the capsule of the organ and in the neighboring connective tissue. Some of the smaller branches of this plexus, the *capsular arteries*, supply the capsule itself, others enter the organ and are distributed to the cortex and to the medulla. The blood supplied to the capsular arteries, after traversing the capillaries, enters small venules which are tributary to the lumbar and phrenic veins. The course of the cortical and medullary vessels has been exhaustively studied by Flint.‡

The *cortical arteries* enter the *zona glomerulosa* where they abruptly break up to form a capillary plexus which occupies the connective tissue between the cell columns. Capillary vessels are continued from this plexus through the intercellular connective tissue of the *zona fasciculata*, where they are in intimate relation

* Proc. Bost. Soc. of Nat. Hist., 1900.

† Anat. Anz., 1902; also Arch. f. mik. Anat., 1904.

‡ Loc. cit.



FIG. 358.—RECONSTRUCTION OF A DOG'S ADRENAL.
a, arteries; v, vein. $\times 25$. (After Flint.)

with the epithelial cells, and reach the zona fasciculata. Here the capillaries are collected into thin-walled venules or sinusoids. These vessels, after some anastomoses, form venous stems which are continued, without further anastomosis, through the medulla to the central veins. The venules of the cortex possess no walls other than their endothelium.

The medullary arteries are also derived from the capsular plexus. They penetrate the cortex, and at the border of the medulla abruptly terminate in a plexus of capillary vessels which lie in the connective tissue stroma and come into intimate relation with the medullary cells. These vessels possess extremely thin walls, their endothelium often being in direct contact with the adjacent epithelium, whose cells frequently impinge upon the lumen of the capillary vessel (see Fig. 93, page 93). The capillary plexus pervades the entire medulla, its vessels being here and there collected into small venules which unite to form the central veins. These form two, or sometimes four, main stems (Flint) which make their exit at the hilum and enter the lumbar or renal vein, or, on the right side, enter the inferior vena cava.

All of the efferent veins of the adrenal are characterized by a peculiar distribution of their smooth muscle fibres, which occur in considerable abundance, but are nearly all disposed in the axis of the vessel; the circular muscle fibres are confined to a very thin coat beneath the endothelium, or are often entirely absent. Frequently, and especially in the central veins of the adrenal, the coarse bundles of longitudinal muscle fibres project into the lumen of the vessel in a somewhat rugose manner. Whenever two veins unite to form a larger vessel, and at the junction of a central vein with any of its branches, these protuberant muscular bundles are especially prominent. Moreover, the author has frequently observed anomalous vessels of a venous nature which arise in the medulla, penetrate the cortex, and enter the venous plexus of the capsule; and in these instances the same peculiar distribution of the muscle has been observed in the veins of the capsular plexus.

LYMPHATICS.—The lymphatics of the suprarenal gland, according to Stilling,* form rich plexuses in the zona glomerulosa and in the medulla; elsewhere they are less abundant. They follow the course of the blood vessels and are especially well developed in the vicinity of the central veins.

* Arch. f. path. Anat., 1887.

NERVES.—The adrenal is well supplied with small sympathetic nerve trunks; in fact, the ontogenetic relations between the adrenal and the large sympathetic ganglia of the solar plexus are extremely intimate, the cells of the medulla apparently taking their origin, in embryos about 3 cm. in length, from the primitive anlagen of the sympathetic ganglia.

The sympathetic nerves form a plexus in the capsule from which branches are distributed to the cortex and to the medulla. In the cortex they invest the blood vessels with a delicate plexus, but have not been found within the epithelial cell columns. In the medulla they are also distributed to the blood vessels and are supplied with occasional small ganglia. From the plexus of sympathetic nerve fibres which invests the groups of medullary epithelium, Dogiel * demonstrated delicate fibrils, supplied with minute varicosities, which penetrate between the epithelial cells and terminate in a manner very similar to that which is characteristic of the epithelial parenchyma of other secreting glands.

II. THE THYROID GLAND.

The thyroid consists of a mass of glandular tubules or follicles, supported by a connective tissue stroma and supplied with a thin but dense fibrous capsule which closely invests the surface of each of its lobes.

The Connective Tissue Framework.—The capsule of the thyroid consists of dense white fibrous and elastic tissue, from which trabeculae, containing the larger blood vessels, pass inward and produce an indistinct lobular subdivision. A network of delicate fibres, among which are very few if any elastic fibres, passes from the trabeculae and invests the glandular follicles, forming a delicate basement membrane for their epithelium. Flint † has shown that much of this interfollicular connective tissue is of the reticular variety. In it are contained the smaller blood vessels and lymphatics. It also contains a few leucocytes, which are scattered about in a diffuse manner.

The follicles of the thyroid are ovoid saccules or short branched tubules with frequent diverticula (Streiff ‡). They vary greatly in diameter and in the calibre of their lumen. Many of them present scarcely any lumen, others appear, from their extreme size

* Arch. f. Anat., 1894.

† Johns Hop. Hosp. Bull., 1903.

‡ Arch. f. mik. Anat., 1897.

(100 to 200 μ), to simulate small cysts. All follicles which possess any considerable lumen contain a peculiar acidophile substance, known as *colloid*, which is apparently formed by the secretory activity of the glandular epithelium lining the follicles.

Colloid is a homogeneous or very finely granular substance which stains readily with eosin, taking a very bright tint closely

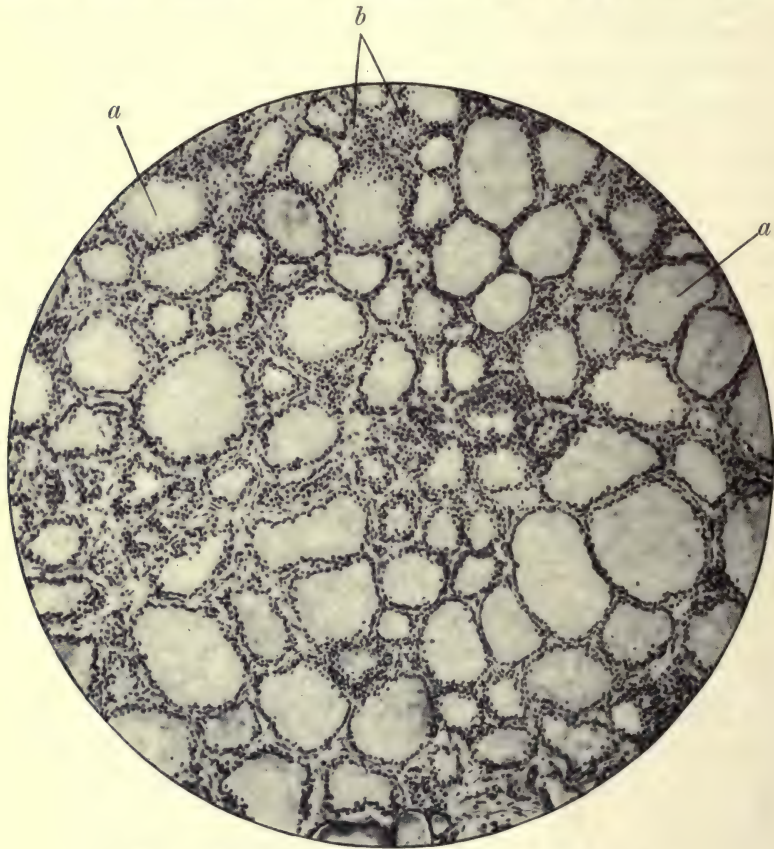


FIG. 359.—FROM A SECTION OF THE HUMAN THYROID GLAND.

a, thyroid follicles in transection; *b*, tangential section of the follicular wall.
Hematein and eosin. Photo. $\times 110$.

resembling that acquired by the hemoglobin of the red blood cells. Frequently, and especially in specimens which have been fixed and hardened in alcohol, it presents a vacuolated appearance. As a rule the lumen of the follicle is not completely filled with

the colloid mass, which is then adherent to the surface of the lining epithelium by delicate thread-like processes; the colloid thus acquires a deceptive appearance of extreme contraction, as if its surface, except for occasional delicate strands, had been drawn away from the epithelium.

Occasionally a single large vacuole, often containing basophile granules or crystalloid particles, occupies the center of the colloid mass in the larger follicles; at other times the colloid material appears to be broken into minute spherules. In general, the ratio of colloid content within the follicle, roughly stated, is in proportion to the age of the individual. The follicles at the periphery of the lobes of the gland are less fully distended than those in the interior.

Embedded in the colloid mass within the follicle, even in the apparently normal thyroid, red blood cells and desquamated follicular epithelium are frequently found, but never in large quantity. Leucocytes are of less frequent occurrence and are more rarely found in the human thyroid than in that of the lower mammals.

The follicular epithelium is typically cuboidal in shape; in young individuals it is somewhat taller than broad. In those follicles which are distended with colloid secretion the epithelium is relatively short; in those which are empty it is taller. Each cell contains a single spheroidal nucleus which lies in the center of the cell, or somewhat toward its basal extremity. This orderly disposition causes the nuclei, when seen in sections of the follicle, to appear as a continuous row in the wall of the alveolus, a disposition which is noticeable for its exceptional regularity.

The cytoplasm of the epithelium is finely granular and decidedly acidophile. It usually contains some coarse granules and very small fatty droplets, which are prone to occupy the extremities of the cells. Minute spheroidal granules which give the color reactions of colloid are also found in the cytoplasm of the epithelial cells. Hürthle,* by staining with the Biondi-Ehrlich mixture, succeeded in differentiating two types of cell, one lightly staining, the "chief cells," the other a darker colloid-containing type which he designated as "colloid cells." These variations probably only represent different stages of secretion in the same epithelial cell type. Minute intercellular canaliculi occur at the angles between adjacent cells.

* Arch. f. d. ges. Physiol., 1894.

The epithelium rests upon a very delicate reticular basement membrane and is in close relation with the capillaries and lymphatic vessels of the interfollicular stroma. Colloid material, similar to that within the follicles, has been repeatedly found within the lymphatic vessels (Baber,* Langendorf,† Hürthle‡) and may be readily demonstrated in most sections of the thyroid. Undoubtedly this does not, however, represent the entire "internal secretion" of the gland.

Blood Supply.—The arteries form a rich plexus in and about the capsule of the thyroid, from which numerous branches penetrate the organ, lying in the connective tissue trabeculae between the lobules; they are distributed to all parts of the gland. They supply a rich capillary plexus in the walls of the follicles. The veins retrace the course of the arteries. The walls of the smaller venules consist only of endothelium, with a very thin coat of elastic connective tissue.

Lymphatics.—The thyroid is very abundantly supplied with lymphatic vessels. These form a plexus of very broad lacunar capillaries in the interfollicular connective tissue, where they stand in intimate relation with the follicular epithelium. From this plexus vessels pass to the interlobular connective tissue, in which they form a second plexus, whence lymphatic vessels pass out of the thyroid in company with the blood vessels and enter the deep cervical lymphatic nodes.

Nerves.—The nerves of the thyroid are derived from the sympathetic and are mostly non-medullated. They accompany the arteries and form a delicate terminal plexus in the walls of the follicles. The finer fibrils of this plexus end in contact with the epithelium. Berkley§ found occasional fibrils which apparently penetrated between the epithelial cells, but his observations have not yet been corroborated.

ACCESSORY OR ABERRANT THYROIDS

These bodies, first described by Zuckerkandl,|| are widely distributed through the connective tissue of the cervical region. They are most frequently found in the course of the embryonic thyreo-glossal duct and in the immediate vicinity of the lateral lobes of the thyroid. They present the appearance of embryonal

* Phil. Trans., 1876.

† Arch. f. Physiol., 1889, Suppl. Bd.

‡ Loc. cit.

§ Johns Hop. Hosp. Rep., 1895.

|| Stuttgart, 1879.

“rests” or remnants of thyroid tissue, but are found in nearly all individuals.

The colloid follicles of the aberrant thyroids are usually small, though, in the larger specimens of these bodies, they may attain as great a size as those of the thyroid itself. The cell columns without colloid are more numerous than in the thyroid gland, giving to the aberrant bodies a decidedly cellular appearance.

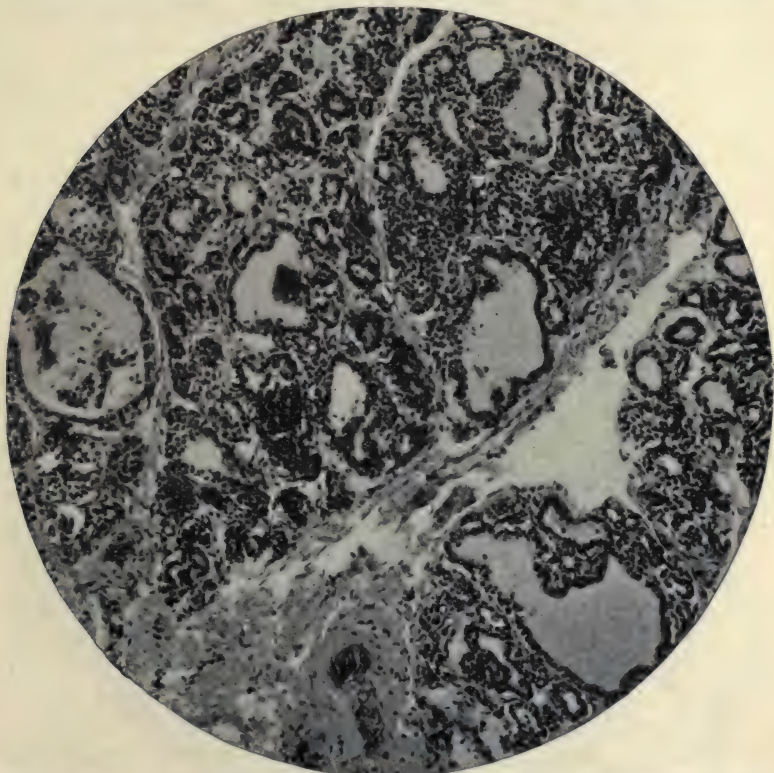


FIG. 360.—FROM THE BORDER OF A MASS OF ABERRANT THYROID TISSUE OF MAN, OCCURRING IN THE REGION OF THE PARATHYROID GLANDS.

Hematein and eosin. Photo. $\times 204$.

Each aberrant mass is usually inclosed by a very thin connective tissue capsule which sends delicate processes between the cell groups. The epithelial cells retain all the characteristics of those of the thyroid gland, and can be readily distinguished from the epithelium of the parathyroid glands with which the accessory

thyroid bodies have been frequently confused. They are also much less vascular than the parathyroids.

III. THE PARATHYROID GLANDS

The parathyroids are small glandular bodies of irregular distribution, usually found in relation with the posterior margin of the lateral lobes of the thyroid gland. Frequently they occur in relation with the tracheal or laryngeal wall and may be found as high

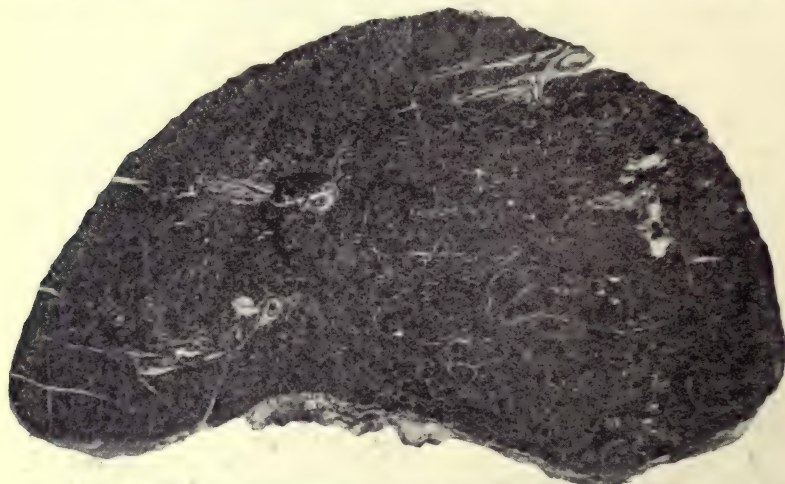


FIG. 361.—TRANSECTION OF A PARATHYROID GLAND OF MAN.
Hematein and eosin. Photo. $\times 10$.

as the hyoid bone or as low as the border of the thymus. In man they are asymmetrical in their distribution, no more than two being present on either side. They also vary greatly in size and shape, but usually are of ovoid form and about 3 to 5 mm. in diameter.

Each parathyroid is invested by a thin capsule of dense connective tissue and consists of a mass of epithelial cells supported by a delicate fibrous reticulum. The epithelial cells are of two chief types, designated by Welsh* as the "principal" and the "oxyphile" or acidophile cells.

The *principal cells* are the more abundant. They are ovoid or spheroidal elements, with a clear vesicular cytoplasm, a distinct cell membrane, and a large spherical nucleus, whose chromatin is irregularly distributed and often gives the nucleus, a somewhat vesicular character.

* J. Anat. and Physiol., 1898.

The *acidophile cells* are of similar shape but are provided with a small spherical nucleus, which is very rich in chromatin, and a granular acidophile cytoplasm. The acidophile are less numerous than the *principal cells*.

The distribution of the epithelial cells is subject to considerable variation. Most frequently they form an almost solid epithelial mass, in which capillary vessels are here and there found, the larger blood vessels occupying the coarser bands of the fibrous stro-

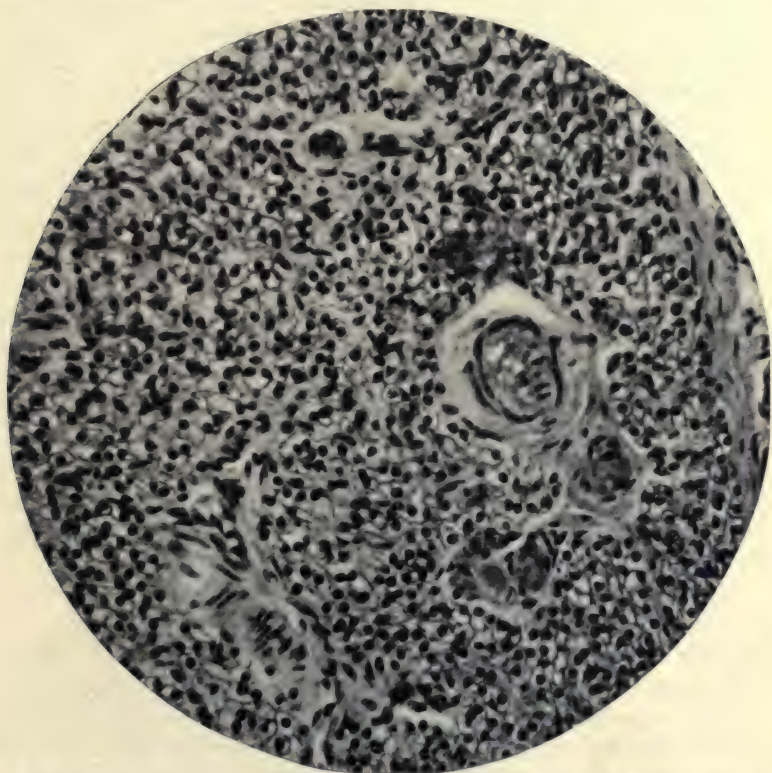


FIG. 362.—FROM A CENTRAL PORTION OF THE PRECEDING FIGURE, SHOWING THE APPEARANCE OF THE CELLS OF THE HUMAN PARATHYROID GLAND UNDER MODERATE MAGNIFICATION.

Several blood vessels are included. Capillary vessels can scarcely be recognized with this magnification. Hematein and eosin. Photo. $\times 300$.

ma. In such glands the two cell varieties are either intermingled irregularly, or the acidophile cells may occur in scattered groups which are interspersed among the more numerous principal cells.

In certain instances the epithelial cells are arranged in small alveolar groups which are surrounded by a network of capillary vessels. This arrangement appears to be more frequent in young individuals. The cell groups in this type of gland frequently form branching columns.

Occasionally, epithelial cells surround a central lumen, in which are small masses of an acidophile substance which resembles colloid in its reactions. In the experience of the author this colloidal material is less abundant in the human parathyroid than in that of the lower mammals. Likewise the cystic ducts, lined by columnar or ciliated columnar epithelium, which have been described by Kohn,* though of frequent occurrence in the lower mammals are rarely, if ever, found in the human parathyroid.

The connective tissue of the gland is of variable quantity. It forms a thin but dense capsule; occasionally trabeculae extend inward and partially outline indistinct lobules. In many instances a hilum transmits the larger blood vessels by means of vascular trabeculae which radiate to all portions of the organ. A delicate fibrous or reticular stroma invests the individual cells, or the cell groups, when these are present. Occasionally the cells are so closely packed that the stroma is scarcely demonstrable.

The blood supply of the parathyroid is exceedingly rich. Arteries enter from the capsule, or at the hilum, and rapidly break up into a plexus of broad capillary or sinusoidal vessels which follow the fibrous bands of the stroma and are in intimate relation with the epithelium. They are collected into thin-walled venules which retrace the course of the arteries.

IV. THE CAROTID GLAND

This body was first carefully described by Luschka † and, from its intimate relation to the blood vessels and nerves, is also known as the *glomus caroticum* or *ganglion intercaroticum*. It consists of scattered masses of epithelial cells, usually grouped in small spheroidal clumps or "*cell balls*," embedded in the connective tissue. Kohn ‡ has described four types of the gland according to the density of its parenchyma—the type found in man consists of scattered cell groups; in the rabbit they are even more diffuse. The carotid gland of a cat consists of a single cell mass, while that of the ape is intermediate between that of the cat and man.

* Arch. f. mik. Anat., 1897.

† Arch. f. Anat., 1862.

‡ Arch. f. mik. Anat., 1900.

The nature and genesis of the glandular cells is somewhat doubtful. They are ovoid elements with finely granular cytoplasm and a spheroidal, somewhat vesicular nucleus. Many of them contain a yellowish pigment which is intensified by fixation in solutions of potassium bichromate (Kohn). This is the so-called *chromofine reaction* which is likewise exhibited by the medullary cells of the suprarenal glands and by many nerve cells.

The carotid gland is richly supplied with capillary blood vessels and small non-medullated nerve trunks. The capillaries are in intimate relation with the glandular epithelium.

V. THE COCCYGEAL GLAND

This small body—2.5 mm. in diameter (Eberth)—was discovered by Luschka* in 1860. Its structure closely resembles that of the carotid gland.

It usually consists of several minute groups of epithelioid cells which are in relation with the terminal branches of the middle sacral artery. It is richly supplied with broad capillaries or sinusoids and hence is also known as the *glomus coccygeum*.

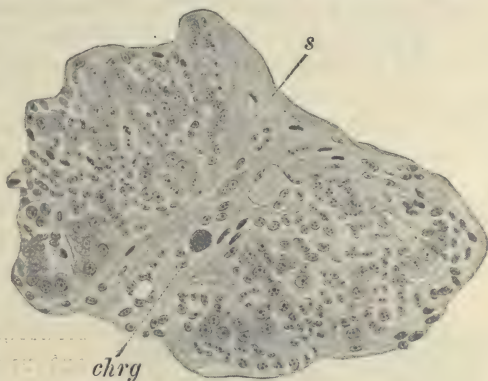


FIG. 363.—CAROTID GLAND OF AN APE.

Chrg, a "chromofine cell"; *s*, connective tissue septum. Portions of two adjacent lobules are included in the figure. $\times 200$. (After Kohn.)

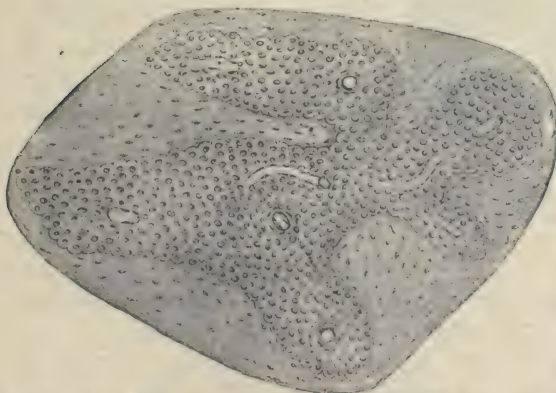


FIG. 364.—FROM A SECTION OF THE COCCYGEAL GLAND OF MAN. Highly magnified. (After Sertoli.)

* Arch. f. path. Anat., 1860.

The parenchymal cells of the organ are ovoid elements which are closely packed about the walls of the blood vessels in groups or short columns inclosed by delicate sheaths of connective tissue. The origin and function of these cells are unknown. The organ is embedded in the dense connective tissue at the tip of the coccyx.

VI. HYPOPHYSIS CEREBRI (*Pituitary Body*)

This body consists of two distinct lobes, an anterior and a posterior. The posterior is largely composed of nerve elements;

the anterior is more distinctly glandular. This difference in structure is doubtless dependent upon the genesis of the organ, the posterior lobe being developed as an outgrowth from the second cerebral vesicle or diencephalon, the anterior arising as a diverticulum from the oral cavity of the fetus.

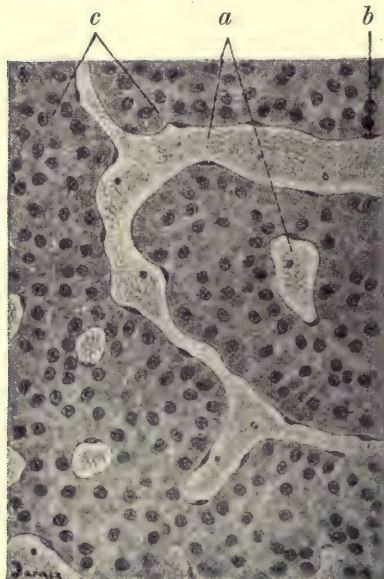


FIG. 365.—FROM A SECTION OF THE HYPHYSIS CEREBRI OF A DOG.

a, blood vessels; b, endothelium of the vascular wall; c, glandular epithelium. $\times 300$. (After Szymonowicz.)

The cellular elements of the posterior lobe include ependyma cells, neuroglia cells, small nerve cells, and a few epithelioid cells (Berkley*). The anterior lobe consists of epithelial cells which occur in small groups and irregular strands, between which are broad sinusoidal capillaries. The cells are ovoid in shape, of a finely granular appearance, and possess large spheroidal

nuclei. Some of them, the *chromophile cells*, are somewhat acidophilic and granular; the *chief cells*, on the other hand, show no special affinity for acid dyes. In this they resemble the cells of the parathyroid gland. Occasionally the cell columns of the pituitary gland assume a tubular or follicular character and in

* Johns Hop. Hosp. Rep., 1895.

these cases the lumen often contains a colloid mass resembling that found in the thyroid follicles.

The organ is richly supplied with blood vessels, which form an extensive capillary plexus among the cell columns and are thus brought into intimate relation with the glandular epithelium. The *nerves* of the anterior lobe, according to Berkley, are derived from the sympathetic, and terminate in varicose end fibrils which are in contact with the epithelial cells. The nerve supply is relatively scanty.

CHAPTER XXIII

THE NERVOUS SYSTEM

A. ITS TISSUES AND DEVELOPMENT

THE nervous system is readily divisible into two anatomical portions, the central and the peripheral.

The central nervous system (cerebro-spinal axis) includes, as its more important gross divisions, the cerebrum or telencephalon, its large basal nuclei (optic thalami, etc.) or diencephalon, the crura cerebri and corpora quadrigemina or mesencephalon, the pons Varolii and cerebellum or metencephalon, the medulla oblongata or myelencephalon, all of which lie within the cranial cavity and are collectively called the brain, and the spinal cord or myelon which is contained within the medullary cavity of the vertebral column.

The peripheral nervous system includes the cranial and spinal nerve trunks with their cerebro-spinal ganglia, and the sympathetic nerve trunks and ganglia, together with their peripheral nerve endings, the motor and sensory end organs. These portions have been already described in Chapters VIII and IX.

Though the above anatomical divisions are macroscopically distinct and are of great convenience in description, it must be borne in mind that the histological elements, the cell units called *neurones*, are not confined to any one gross division, but may, as a nerve cell with its many processes, be traced in direct anatomical continuity through several such gross divisions. Some neurones, for example, whose cell bodies lie in the posterior root ganglia of the spinal nerves may be followed throughout a peripheral nerve trunk on the one hand, while on the other it sends a process centralward which enters the spinal cord and passes all the way to the medulla oblongata.

The central nervous system is said to consist of grey and white matter, the grey matter being composed chiefly of *nerve cells* with

their non-medullated processes, the white matter containing only the medullated processes of the nerve cells, which are known as *nerve fibres*.

THE SUPPORTING TISSUES OF THE CENTRAL NERVOUS SYSTEM.—Both the grey and the white matter of the central

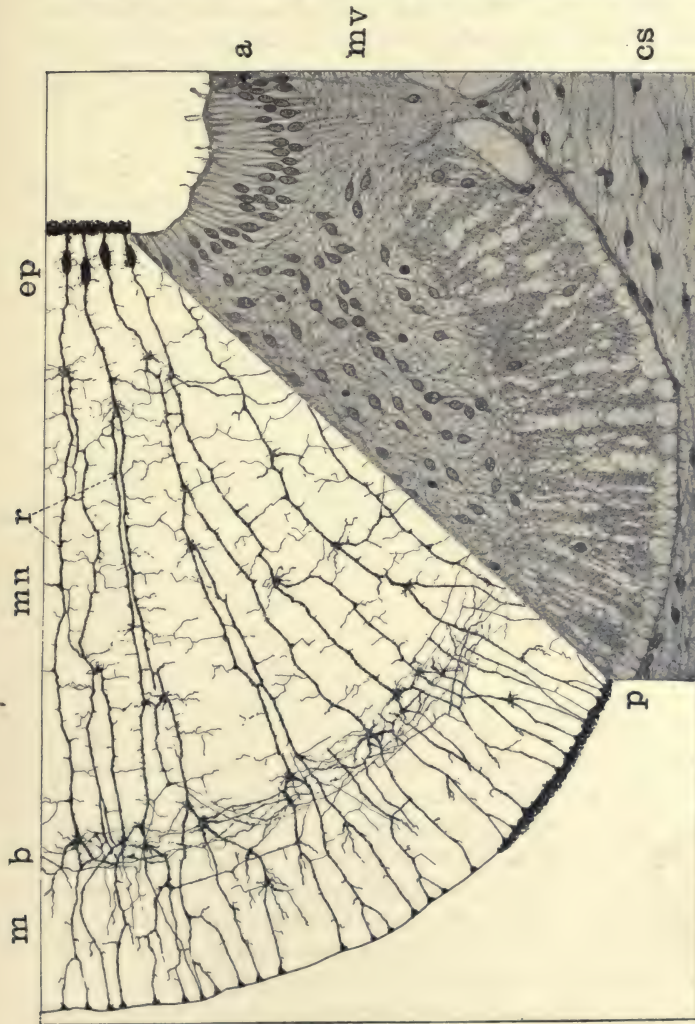


FIG. 366.—NEUROGLIA FROM THE SPINAL CORD OF A FETAL PG.

The portion above shows the result of the Golgi stain; below, that of a hematein and Congo red stain. *a*, inner layer of neuroglia, adjoining the central canal; *b*, boundary between the nucleated and mantle layers of neuroglia; *cs*, connective tissue; *ep*, ependyma; *m*, mantle layer; *mn*, middle or nucleated layer of neuroglia; *mv*, ventral raphe; *p*, pia mater; *r*, radial filaments of the neuroglia. $\times 320$. (After Hardesty.)

nervous system contain a peculiar supporting tissue, the *neuroglia*, which consists of two elements, the glia cells and the glia fibres.

The latter are very probably produced by the glia cells, of which they were formally considered to be processes.

The **glia cells**, as seen in Golgi preparations, are divisable into two distinct types, the ependyma cells and the astrocytes.

The *ependyma cells* may be considered as undifferentiated relics of the embryonal cells, from which both glia and true nerve or ganglion cells were presumably developed. These cells line the central canal of the spinal cord and the ventricles of the brain, in which latter organ they also form the covering or outer coat of the *telae choroidei*.

The ependyma consists of long nucleated columnar cells whose free ends, in fetal and early life, carry a tuft of cilia; in adult life

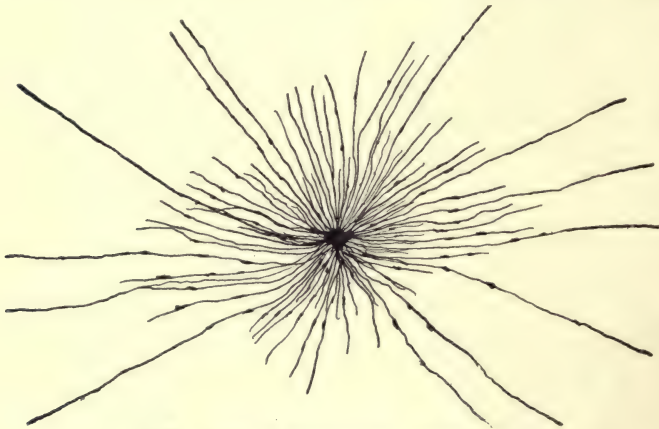


FIG. 367.—A LONG-RAYED ASTROCYTE.
Golgi's stain. Highly magnified. (After Berkley.)

they are usually non-ciliated. The attached ends of these cells are embedded in the surrounding gelatinous tissue, and are frequently prolonged for some distance as a fine branched process. In this way the ependyma of the spinal cord enters into the formation of the *substantia gelatinosa centralis*, in which the branched processes of its cells ramify in a glia-like manner. In the fetus the filamentous processes extend from the central canal all the way to the periphery of the spinal cord. In the adult the ependyma cells are prone to so multiply as to almost occlude the central canal; their processes have apparently become shorter, and now reach the surface of the spinal cord only at its posterior median sulcus.

The *astrocytes* (Deiter's cells), when stained by the Golgi method, apparently consist of a small cell body and an innumerable number of long slender processes. Two varieties of these cells are recognized; the *spider cell* or *long-rayed astrocyte*, with a small cell body and very many exceptionally long and slender processes; and the *mossy cells* or *short-rayed astrocytes*, whose processes are shorter and somewhat thicker but decidedly more varicose than those of the long-rayed type.

Recent investigations by means of the staining methods of Weigert, Mallory, and Benda, have demonstrated that the astrocytes, as seen in the Golgi preparations, probably include two distinct structures, the glia cells and the glia fibres.

Glia cells, as seen in sections prepared according to these methods, appear as small cytoplasmic cells with large and deeply staining nuclei. In the small glia cells the cytoplasm is so slight as to form scarcely more than a mere rim about the nucleus; in the larger cells the cytoplasm is more abundant and the processes larger and more numerous. The presence of cytoplasmic processes gives the cell an irregularly stellate appearance. In Golgi preparations these processes can not be distinguished from the dense network of glia fibres with which they are surrounded.

The *glia fibres* comprise numerous filiform fibrils which occur as a dense network around the glia cells, from which they radiate in all directions. They pass alongside of, over, or under the glia cells; their filaments have even been described as passing entirely through the cytoplasm of the cell. Nevertheless they appear at all points to be anatomically distinct from the cell body.

The relation of the glia cells to the fibres of neuroglia is perhaps comparable to the arrangement in fibrous or reticular tissue. The fibres of each of these tissues appear to be ontogenetically derived either directly or indirectly from its cells, yet when fully formed they often exist as anatomically distinct elements.

Neuroglia cells and fibres occur in both the grey and white matter of the central nervous system, though perhaps more abundant in the latter. The fibres radiate for considerable distances from their glia cells, and thus form a supporting tissue for the

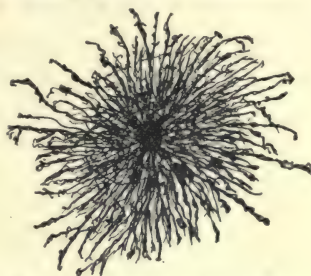


FIG. 368.—A SHORT-RAYED ASTROCYTE, OR MOSSY CELL.

Golgi's stain. Highly magnified.
(After Berkley.)

nerve elements. They are frequently in intimate relation with the blood vessels, on the walls of which many of the glia fibres, particularly the thicker or mossy cell variety, terminate in ex-

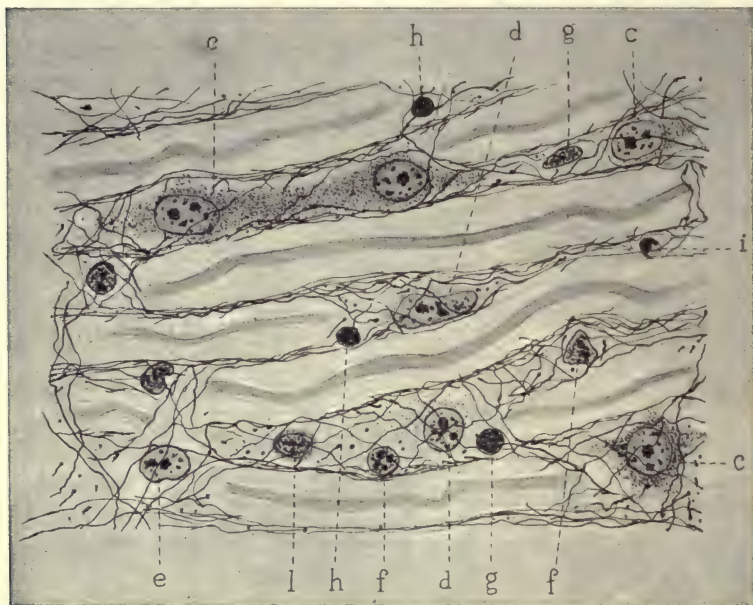


FIG. 369.—NEUROGLIA CELLS AND FIBRES FROM THE SPINAL CORD OF AN ELEPHANT. The letters indicate various types of neuroglia cells. *l*, a leucocyte. Benda's stain. $\times 940$. (After Hardesty.)

panded plates, which, in some parts, form an almost complete outer membranous coat of the vessel.

The astrocytes are ontogenetic derivatives of the embryonic ependyma cells. From their point of origin around the neural canal they wander to all portions of the central nervous system, and even into the optic and olfactory tracts, which are embryonic outgrowths from the fetal cerebral vesicles. Thus neuroglia occurs throughout the brain and spinal cord, and also in the olfactory nerves, the optic chiasm, and the retina of the adult.

The supporting tissues of the central nervous system include, besides the neuroglia, numerous bands or trabeculae of fibrous connective tissue, which push inward from the pia mater, carrying with them the vascular branches for the supply of the nervous tissues, and which penetrate deeply into the substance of the spinal cord and brain.

THE NEURONE.—The nerve elements of the central, as well as the peripheral, nervous system include the *nerve cells* and the nerve cell processes; the latter are usually called *nerve fibres*. This subdivision, which has been handed down from former times, when it was considered that nerve cells and nerve fibres were independent elements, is still useful for descriptive purposes. However, it must be constantly borne in mind, and can not be too often emphasized, that these two terms are merely descriptive of two portions of the same anatomical unit, the neurone.

Thus the neurone forms the structural unit of the entire nervous system. This unit has already been discussed in its relation to the nervous tissues,* but the importance of a correct impression of its bearing on the structure of the central nervous system as at present interpreted, makes it advisable at this time to briefly review its structure.

A neurone is an animal cell. It consists of a cell body (*nerve cell, ganglion cell, perikaryon*) with all of its various processes. These processes include the dendrites, which are considered as usu-

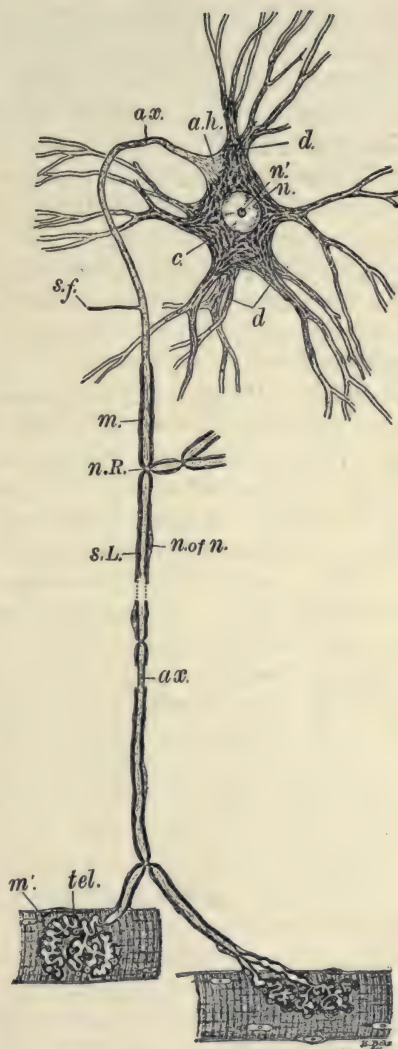


FIG. 370.—DIAGRAM OF A NEURONE.

ah, axon hillock; ax, neuraxis; c, cytoplasm; d, dendrites; m, myelin sheath of the nerve fibre; m', muscle fibre; n, nucleus; n', nucleolus; n. of n, nucleus of the neurilemma; nR, node of Ranvier; sf, collateral; sL, segment of Lantermann; tel, telodendrion. (After Barker.)

* See Chapter VIII.

ally transmitting cellulipetal impulses, and the neuraxes and collaterals, which transmit cellulifugal impulses. The cell body or nerve cell has already been sufficiently described.*

The *dendrite* is a broad arborizing process whose substance closely resembles the cytoplasm of the cell body in its microscopical appearance and in its staining reactions. It branches freely, but always dicotymously, and usually ends at a point not very remote from its cell body.

The *neuraxis* (*nerve fibre*, *axis cylinder process*, *axon*, *dendron*, *neurite*, etc.) is a long and slender process. It arises either directly from the cell body or indirectly from the trunk of one of its dendrites. It gives off numerous *collaterals* at right angles to the parent fibre throughout the greater part of its course, and finally terminates, as do also its collaterals, in an *end brush* (*terminal arborization*, *felt work*, *basket work*, etc.), or in one of the several forms of peripheral nerve end organs.

The end brushes are apparently formed by the rapid separation of the fibre into its component fibrillae.

The neuraxis is usually a much longer process than are the dendrites. Unlike the latter, it extends not merely to other portions of the grey "*nucleus*," in which its cell body lies, but frequently it passes without interruption of its anatomical continuity to other and even very distant parts. The wide radius through which these fibres are distributed is well illustrated by the passage of neuraxes, coming from nerve cells of the cerebral cortex, to the grey matter of the spinal cord; other nerve cells in the spinal cord send their neuraxes through the entire length of the spinal nerve, to supply even the most remote tissues of the body. While, therefore, the cell bodies and dendrites are measured in millimetres or micromillimetres, the neuraxis is often to be measured only in centimetres and decimetres. There are very few cells in the body which are in any way comparable to the nerve cell or neurone for the large size of its cell body and the extensive area of distribution of its processes.

All portions of the neurone, its neuraxis and collaterals as well as its dendrites, are dependent upon the cell body for nutrition; hence each nerve cell becomes the so-called *trophic center* for all of its processes.

The entire nervous system may be considered as an enormous tangle, formed by the interlacing processes of an innumerable

* Chapter VIII.

number of neurones whose complex fibre paths place all portions of the body in communication with all other portions.

Nerve cells are unequally distributed throughout the central nervous system; they therefore occur in more or less distinct groups or *nuclei*, from each cell of which a neuraxis is frequently distributed along the same path. The larger bundles thus formed are called *tracts*; the smaller ones, *funiculi*, *fasciculi*, or *fibre bundles*.

Since each fibre of such a tract is dependent for nutrition upon the nerve cell from which it arises, the tract as a whole must depend upon its nucleus of origin for its nutrition. Each nucleus therefore becomes the trophic center for the fibre tract to which it gives origin.

It may be readily demonstrated that if any such group of neuraxes be cut or otherwise separated from its trophic center, that tract will promptly degenerate. If these neuraxes happen to be the axis cylinders of medullated nerve fibres, as is often the case, their myelin sheaths become rapidly altered in composition and acquire a tendency to disintegrate into small globular granules, which stain deeply with osmic acid when used according to the method of Marchi. For the experimental demonstration of this form of partial cell death occurring in that portion of the neurone which has been cut off from its cell of origin, we were originally indebted to the eminent English physiologist Waller; the resulting changes are therefore called *Wallerian degeneration*.

Obviously that portion of a neurone or of a fibre tract which, after injury or disease involving its path, still retains its connection with its cell body or trophic center, will not degenerate. This part of the neurone is called its *central portion*, in contradistinction to its *distal portion*, the latter of which has been severed from its trophic center and is consequently degenerated.

To the study of the various types of Wallerian degeneration we are indebted for many of the facts by means of which the intricate tangles of neuraxes composing the various fibre tracts of the central nervous system have been partially unraveled.

The Anatomic Relations of the Neurone.—The many neurones in the nervous system are in relation with one another through their neuraxes, collaterals, and dendrites, and by their peripheral processes are closely connected with all the organs and tissues of the body. Our former conception regarded the processes of any one neurone as being nowhere in direct anatomical connection with

those of any other neurone nor with any other tissue within the body; their relation to one another is as a rule one of contiguity rather than of anatomical continuity.

The observations of Apáthy, Bethe, Held, and others, have demonstrated that neurofibrils are at times continued from one neurone to another. But while these observations serve as an important addition to our knowledge of the histology of the nervous tissues, they do not materially alter our conception of the neurone as an anatomical unit of the nervous system, any more than the occasional occurrence of a syncytium modifies our views of the cell as an anatomical unit of body structure. The neurone is a nerve cell in the broadest sense of the term.

The connection existing between the several tissue elements of the body and the peripheral neuraxes of the nervous system takes place through the intervention of the nerve end organs, motor and sensory, in nearly all the tissues of the body, at the peripheral terminations of the nerve fibres. These end organs have been described in a previous chapter, and will not need further discussion at this time.

The contiguous relationship of different neurones within the nervous system occurs in any one of several ways. The terminal arborizations or end brushes of one neurone may interlace with:—

- a. the end brushes of neuraxes belonging to other neurones,
- b. the end brushes of collaterals of other neurones,
- c. the dendrites of other neurones, or
- d. the terminal arborization may surround, basket-like, the cell body of other neurones.

Golgi Cell Types.—The length of the neuraxis varies greatly in different neurones. Dependent upon this fact, as demonstrated in preparations by the staining method of Golgi, nerve cells have been classified into two cell types, Golgi cells, Type I, and Type II.

- a. *Golgi cells, Type I*, viz., those having long neuraxes.

The neurones of this type send their neuraxes beyond the confines of the grey nucleus in which their cell bodies lie and in which their dendrites are distributed. Such, for example, are the peripheral motor neurones whose cells lie in the spinal cord, and whose neuraxes are distributed to the various muscles of the body; such also are the central motor neurones whose cells lie in the cerebral cortex, and the end brushes of whose neuraxes surround the cell

bodies of the peripheral motor neurones in the spinal cord. Cells of this type are familiarly known as the "*Deiters' cells*."

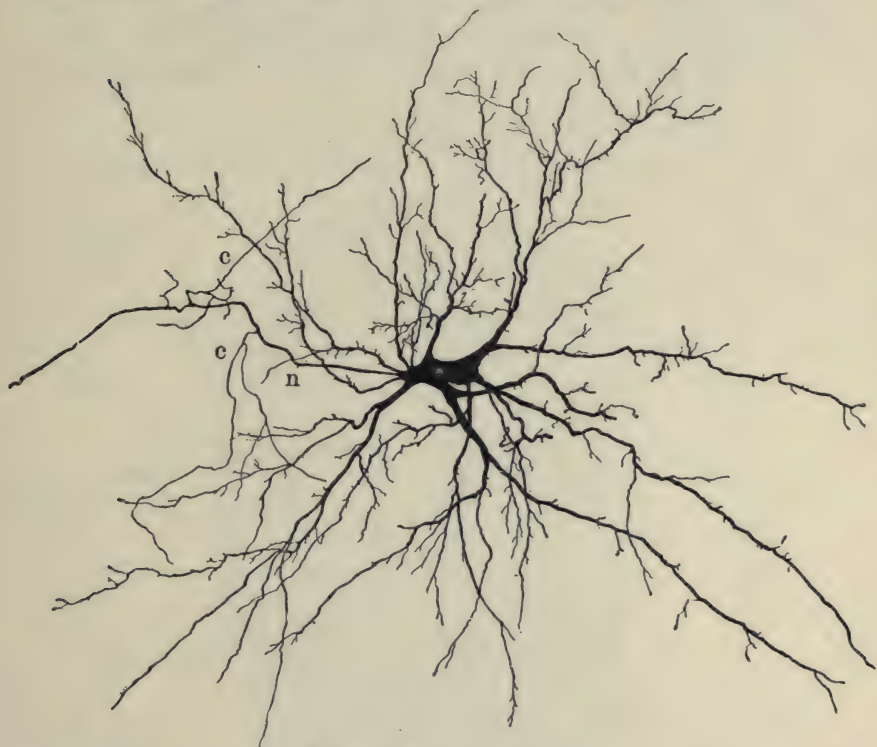


FIG. 371.—GOLGI CELL, TYPE I.

c, collaterals; n, neuraxis. Golgi's stain. (After Kölliker.)

b. Golgi cells, Type II (Golgi cells), viz., those having short neuraxes.

The neuraxes of cells of this type do not leave the grey nucleus in which they take origin. Their branching begins almost immediately and their end brushes are found in the immediate vicinity of their cell body. These cells undoubtedly serve to place neighboring neurones in close physiological relation, whereas the cells of the first type connect distant parts.

The size of a nerve cell is thought to bear a general relation to the length of its neuraxis, the larger cells possessing the longer neuraxes. The cells of Golgi's Type I are therefore larger than those of Type II. Likewise the cells of the motor tracts, whose

neuraxes are as a rule much longer than those of the sensory tracts, are characterized by their large size as compared with the sensory cells.



FIG. 372.—GOLGI NERVE CELL, TYPE II.
a, neuraxis; *x*, dendrite. (After Kölliker.)

DEVELOPMENT OF THE NERVOUS SYSTEM

A familiarity with the principal stages in the course of the development of the nervous system is necessary for the proper appreciation of its histology.

The appearance of the first anlage of the nervous system occurs

at a very early stage of embryonic life; is, in fact, the first differentiation which can be observed after the subdivision of the blastoderm into its three primary layers. The epiblast very early presents a shallow longitudinal groove bordered on either side by a slight ridge; this is the *neural groove*, bounded by its *neural ridges*.

The ectodermal cells forming the neural ridges multiply much more rapidly than those lying in the bottom of the groove; conse-

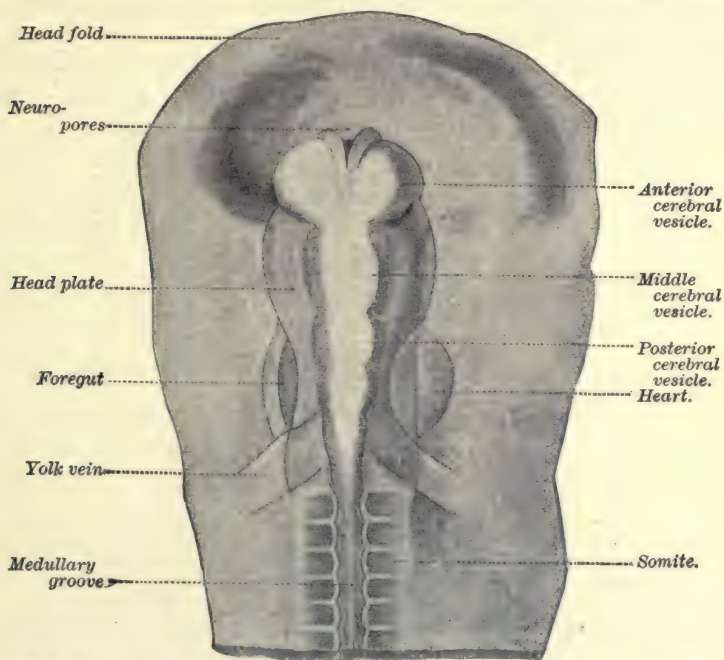


FIG. 373.—RECONSTRUCTION OF THE ANTERIOR PORTION OF THE BODY OF A CHICK, THE HEAD DISTINCTLY DIFFERENTIATED, SEEN FROM THE SURFACE. (After Kollmann.)

quently the ridges come more and more to overhang the groove, and by continued growth they finally meet along the median line. The opposed surfaces of the two lateral ridges then fuse together and the former groove becomes a tube, the *neural canal*, which is at first much flattened from side to side, its ventro-dorsal being considerably greater than its transverse diameter. At this stage the neural canal resembles a long axial slit bounded upon all sides by epiblastic cells.

The caudal portion of the neural canal is destined to become

the central canal of the spinal cord, its cephalic portion forms the cerebral vesicles. The former portion retains an approximately equal caliber throughout; the latter soon presents three characteristic dilatations, the three *primary cerebral vesicles*, whose walls respectively develop the *prosencephalon*, *mesencephalon*, and *rhombencephalon*.

The first and third of these primary cerebral vesicles soon subdivide into two each, five *secondary vesicles* being thus formed. These five vesicles are the *telencephalon*, *diencephalon*, *mesencephalon*, *metencephalon*, and *myelencephalon*.

The following table exhibits the relation of the several primitive vesicles to each other as well as to the gross divisions of the central nervous system :

NEURAL CANAL	{	ENCEPHALON (brain)	{	I. PROSEN- CEPHALON (forebrain)	{	I. TELENCEPHALON (endbrain)		
				II. DIENCEPHALON (interbrain or 'tweenbrain)				
			{	II. MESEN- CEPHALON (midbrain)	{	III. MESENCEPHALON (midbrain)		
		{		III. RHOMBEN- CEPHALON (rhomboid brain)		IV. METENCEPHALON (hindbrain)		
						V. MYELENCEPHALON (afterbrain)		
	{		MYELON (spinal cord)					

The encephalon develops the various portions of the brain, the cranial nerves and their ganglia. The myelon forms the spinal cord, the spinal nerves and their ganglia. The sympathetic nerves and ganglia are outgrowths from the cerebro-spinal nerve roots.

The following lists will show more definitely the destination of the several portions of the encephalon and the parts of the brain formed from each of the cerebral vesicles.

1. **From the Telencephalon.**—The anterior end of the third ventricle, the lateral ventricles, the foramen of Monroe, the cerebral hemispheres with their cortex or pallium, the olfactory bulb and its tracts (sometimes called the *rhinencephalon*), the corpora striata, the corpus callosum, and the fornix.

2. **From the Diencephalon.**—The third ventricle, the optic nerve and retina, the optic tracts (*pars optica hypothalmi*), the optic

thalamus, the cerebral portion of the pituitary gland, the pineal gland, and the corpora mamillaria.

3. **From the Mesencephalon.**—The corpora quadrigemini, the crura cerebri (pedunculi cerebri), and the aqueduct of Sylvius.

4. **From the Metencephalon.**—The isthmus rhombencephali, pons Variolii, and cerebellum.

5. **From the Myelencephalon.**—The medulla oblongata.

The Ependyma.—The epiblastic cells which line the lateral walls of the slit-like neural canal become elongated or columnar in shape, and are called *ependyma cells*. Many of these are germinal cells, exhibiting the various stages of mitosis; the resulting cells promptly differentiate into two distinct varieties, the spongioblast and the neuroblast.

The *spongioblasts* are long cells whose expanded bases line the neural canal and whose elongated bodies are directed outward toward the surrounding mesoblastic tissue. The interlacing processes of these cells, together with those from the neuroblasts, form a network or neurospongium. The spongioblasts are destined to develop the neuroglia.

The *neuroblasts* are small ovoid or fusiform cells, which, though usually bipolar, very early develop a long peripheral process directed away from the neural canal; this process is the primitive neuraxis. In those cells which are to form the nerve roots and the peripheral ganglia this process grows outward into the surrounding mesoblast, the cell gradually migrating along the same course, but leaving in its wake the developing central process which in some cases is dendritic in character, but in others is destined to form a second centrally directed branch of the neuraxis.

It is by means of this property of locomotion that these cells reach their destination in the various cell groups or nuclei in the brain and spinal cord or in the peripheral ganglia. In this way the fibre paths or tracts of the central nervous system as well as the cranial and spinal nerves and their ganglia are formed.

Since, during the period that the neuroblast is performing this migration, it is also developing its neuraxis and dendrites, by the time it reaches its permanent location its principal portions, cell body, neuraxis, and dendrites are already formed and are ready to functionate. The further history of the neuroblast is merely one of continued growth, pushing forward its neuraxis to still more distant and more complex relations.

The development of the posterior nerve root ganglia forms a striking example of the history of the neuroblast, as above described. The manner in which these cells are derived from cells lying in the wall of the neural canal can be readily appreciated by examining successively Figures 374 to 376. After their development has been completed each of these neurones comprise a nerve cell situated in the posterior nerve root ganglion of a spinal nerve, from which one branch of its T-shaped process passes through the spinal nerve toward the periphery, while the other branch, through the posterior root, enters the spinal cord to terminate in its central grey matter either at or near the level at which it enters, or possibly at a much higher and more remote level.

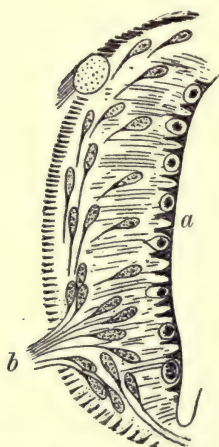


FIG. 374.—DIAGRAM OF A TRANSECTION OF THE SPINAL CORD OF AN EARLY EMBRYO, SHOWING THE MIGRATION OF NEUROBLASTS TOWARD THE MARGINAL VEIL AND THE DORSAL NERVE ROOT.

a, neural canal; *b*, dorsal root.
(After His.)

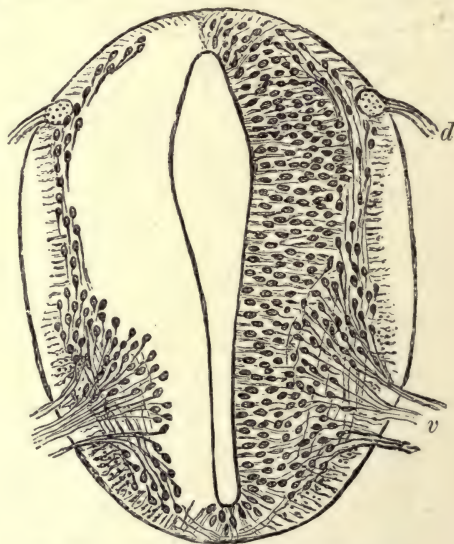


FIG. 375.—TRANSECTION OF THE SPINAL CORD OF A HUMAN EMBRYO OF FOUR WEEKS.

The central canal is immediately surrounded by ependyma cells. The peripheral nerve cells are shown on the left of the figure. The nerve roots are already pushing outward from the primitive cord. *d*, dorsal; *v*, ventral nerve roots. (After His.)

Myelinization.—Having attained its full area of distribution, the last change in the neurone to mark the completion of its development is the appearance of its myelin or medullary sheath. The period at which this sheath is obtained varies with the different tracts of fibres in the nervous system, and seems to be syn-

chronous with the appearance of their function. Thus those neurones, e. g., the peripheral sensory neurone, which in the fetus are first acted upon by stimuli from without, are the first to obtain a

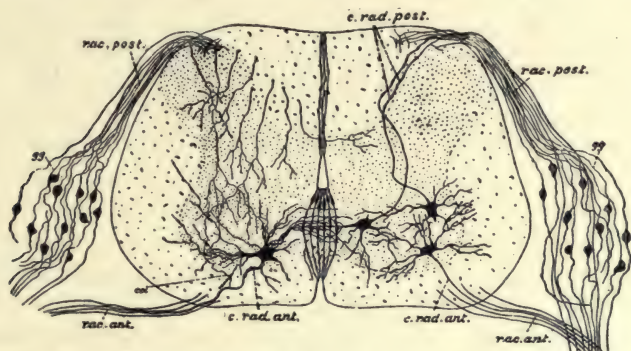


FIG. 376.—TRANSECTION OF THE SPINAL CORD OF AN EMBRYO CHICK.

c. rad. ant., neuraxes to the ventral roots; *c. rad. post.*, neuraxes to the dorsal roots; *col*, collateral from a neuraxis back to the grey matter; *gg*, dorsal root ganglion; *rac. ant.*, ventral root; *rac. post.*, dorsal root. (After van Gehuchten.)

myelin sheath. Following these, medullary sheaths are formed in the peripheral motor neurones, and reflex movements begin; still later, myelin sheaths appear in the intrinsic neurones of the paths of the spinal and cranial nerves which conduct sensory impulses toward the brain; and finally, the cerebral sensory and motor neurones receive their myelin sheaths, and consciousness and voluntary movements are manifested.

To this peculiarity in the formation of the medullary sheaths, as well as to the phenomena of Wallerian degeneration, we are indebted for much of our knowledge of the course of the fibre tracts in the central nervous system. If, for example, sections from the spinal cord of embryos of suitable age be stained to show their myelin sheaths, certain tracts or fibre bundles will be found to have already acquired their medullary coat, while in other bundles the myelin has not yet made its appearance. Thus in a fetus at the seventh or eighth month the sensory paths of the spinal cord will be found to be well medullated, while the adjoining motor paths show scarcely any myelinization.

This method of study, the *myelinization method*, together with the *degeneration method* and the staining methods of Golgi, have supplied most of our knowledge concerning the course of the intricate fibre paths of the brain and spinal cord.

CHAPTER XXIV

THE NERVOUS SYSTEM (*Continued*)

B. HISTOLOGICAL MORPHOLOGY

THE spinal cord and brain collectively form a long slender mass consisting of conduction paths or fibre tracts, which are for the most part axially disposed and connect more or less distant groups of nerve cells. Each cell group controls the functions of a limited portion of the body, to which its neuraxes pass in bundles that follow definite paths. These paths are the so-called *tracts*, and the cell group which gives origin to the fibres of any one tract is its *center* or *nucleus*.

The cerebro-spinal axis is thus composed of many series of such nuclei with their connecting tracts; the nuclei collectively forming the grey, and the tracts the white matter. Except for the cortex of the cerebrum and of the cerebellum the grey matter is, as a rule, centrally, and the white matter peripherally disposed.

Thus in the spinal cord the grey matter consists of a central H-shaped mass extending from the filum terminale upward to the medulla. Above this level the continuity of the central grey mass suffers frequent interruption from the irregular and oblique disposition of the fibre tracts of this region, so that above the medulla the grey matter is only represented by a series of islands (nuclei), each containing one or more cell groups.

In the cerebrum and cerebellum these central nuclei are separated from the grey matter of the cortex by an intervening stratum of white matter; in these locations the larger mass of grey matter is found on the surface of the white medulla.

The peculiar disposition of the grey matter of the brain is explained by the progress of its development. In the early embryo the cerebral vesicles are at first surrounded by a cell mass only. From these cells the fibre processes grow out, and in so doing the excessive formation of fibres at the cephalic end cuts off the grey matter of the cortex (pallium) from the more caudal portions.

This separation is increased by the growth into the cerebrum of the centripetal fibre paths coming into the brain from the more caudal parts.

The grey matter of the cerebral cortex may thus be said to represent a cephalic mantle or covering, which, by its stem of nerve fibres, is supported above the cephalic end of a grey axis of nerve centers which extends from the base of the cerebrum through the midbrain and medulla oblongata to the spinal cord.

This cerebro-spinal axis is developed in two symmetrical halves, which are more or less completely separated from each other by two series of deep sulci or fibrous septa, the one dorsal and the other ventral. In the brain the dorsal is a deep sulcus, the ventral a mere fibrous septum or raphé. In the spinal cord the condition is reversed, the anterior or ventral median fissure forming a deep sulcus, while the posterior is a shallow groove deepened by a prominent median septum.

The cerebro-spinal axis will be best appreciated by a study of its several regions, in succession, from below upward. The following subdivisions are convenient for purposes of description :

SPINAL CORD (<i>myelon</i>)		{	1. Sacral region	
			2. Lumbar region	
			3. Thoracic (dorsal) region	
			4. Cervical region	
BRAIN (<i>cephalon</i>)	{	a. Myelencephalon—	5. Medulla oblongata	
		b. Metencephalon—	6. Pons Varolii	
		{	7. Cerebellum	
			c. Mesencephalon—	8. Region of the cruræ cerebri (brain-stem)
			d. Diencephalon—	9. Region of the optic thalami (basal nuclei)
			e. Telencephalon—	10. Cerebral cortex (pallium)

THE SPINAL CORD (Figs. 377 to 381).—The spinal cord consists of a considerable mass of central grey matter which is surrounded by a layer of nerve fibres, the white matter.

The grey matter consists of two lateral portions united by a central *commissure* (*grey commissure*, *posterior commissure*). Each lateral portion includes an anterior and a posterior *horn* with an intervening deeper portion, the central mass or "*intermediate zone*" of Golgi.

The anterior is somewhat broader than the posterior horn. Its cells supply neuraxes, which, after uniting into bundles, pass ventralward through the white matter to form the ventral (anterior) *nerve roots*.

The spinal cord may be considered as consisting of ontogenetic *segments* whose number corresponds to the number of the spinal nerves. Hence each segment contains the anterior horn cells whose neuraxes form the ventral root of the corresponding spinal nerve.

In an entirely similar manner the posterior horns of the grey matter receive a large portion of the incoming fibres of the posterior roots, which in large part form end brushes around the cells of the dorsal horns and the intermediate zone.

The dorsal roots enter through a distinct longitudinal groove, the postero-lateral sulcus. At the exit of the ventral roots there is, however, only a broad shallow indentation, these roots making their exit in isolated bundles distributed through a vertical plane of considerable width. The dorsal root fibres of each segment, on the other hand, enter in a single compact mass.

The grey matter consists of a dense tangle of nerve cells and fibrils, together with neuroglia and blood vessels. The fibrils of a given area are derived not only from nerve cells in their immediate vicinity, but also include many processes which come from very distant regions. The grey reticulum is thus supplied from fibres of the ventral and dorsal nerve roots, together with innumerable collaterals, not only from the root fibres, but more especially from those fibres which collectively form the many large tracts passing up and down the spinal cord and placing each segment in communication with many other levels of both the spinal cord and brain.

The center of the grey commissure contains the *central canal* which lies in the axis of the spinal cord and is continuous above with the ventricles of the brain. It represents the remains of the fetal neural canal; and in the young subject is still patent, filled with cerebro-spinal fluid, and lined by columnar cells which are frequently ciliated. In older subjects the cells of the lining epithelium have usually lost their cilia, and the lumen of the canal is more or less filled by cell proliferation which involves not only the lining epithelium but also the surrounding glia cells and fibroblasts.

The central canal is immediately surrounded by a peculiar gelatinous tissue in which are many glia cells. This mass is called the *substantia gelatinosa centralis*. A similar area of gelatinous tissue occurs near the dorsal extremity of the posterior horns, and is called the *substantia gelatinosa posterior* or *gelatinous substance of Rolando*.

The white matter forms a covering or shell around the central grey mass. It increases in thickness from below upward. This peculiarity is the result of the constant addition of centripetal fibres, and a corresponding loss of centrifugal fibres, through the spinal nerves of each successive segment.

The posterior median septum extends inward from the shallow sulcus on the dorsal surface of the spinal cord to the central grey commissure, and divides the posterior mass of white matter into two dorsal white columns, lying on either side of the median line, and bounded laterally by the dorsal horns of grey matter and the dorsal nerve roots. The anterior median sulcus in a similar manner, splits the ventral portion of white matter into the two anterior white columns. This sulcus, however, does not penetrate all the way to the grey commissure but leaves an interval of white matter containing many transverse and obliquely disposed nerve fibres. The ventral or *white commissure* thus formed connects the two anterior columns of white matter.

The spinal cord is thus divided into two lateral and symmetrical halves by a plane passing through the anterior and posterior median fissures and the central canal. Each lateral half includes a central mass of grey matter completely surrounded, except at the grey commissure, by the white matter. The latter is subdivided into an anterior, lateral, and posterior column, each of which extends the entire length of the spinal cord and is apparently (to the naked eye only) continuous above with a similar column in the medulla oblongata.

The *anterior white column* is included between the anterior median sulcus and the ventral grey horns and nerve roots; the *lateral columns* extend from the ventral roots in front, around the lateral surface of the spinal cord, to the dorsal roots; the dorsal or *posterior columns* are included between the dorsal horns of grey matter and dorsal nerve roots, and the posterior median septum.

Each of these columns of white matter is again subdivided by connective tissue septa of variable size and number, which extend inward from the pia mater for a considerable distance. Such septa may even penetrate all the way to the central grey matter. One of these septa, more constant than the others, subdivides the posterior column into two portions, a *postero-internal* and a *postero-external column*.

The larger blood vessels are distributed along the fibrous septa, taking their origin from the vessels of the pia mater; the most of

them are distributed to the white matter, but to some extent they also supply the grey matter.

The entire surface of the spinal cord presents, just beneath the pia mater, a thin superficial layer or *marginal veil* of glia tissue. In the brain this layer is somewhat exaggerated in thickness.

THE REGIONS OF THE SPINAL CORD.—The varying number of fibres which are given off at different parts of the spinal cord results in considerable differences in size in its several portions. By means of these peculiarities, as well as by the spinal nerve roots to which they give origin, we distinguish a sacral, lumbar, thoracic, and cervical region. Each of these regions presents certain more or less important morphological characteristics.

In the **sacral region** the investment of white matter is very thin, the grey matter—though actually less in amount than in the more cephalad regions—appearing large by comparison. Both the ventral and dorsal horns of grey matter are short and thick. The substantia gelatinosa of Rolando is of considerable volume. The cell groups in the ventral horns of this region are a *ventro-medial* and a *dorso-lateral*.



FIG. 377.—TRANSECTION OF THE SPINAL CORD OF A CHILD, THIRD SACRAL SEGMENT.

Weigert stain. $\times 7$.

The cord as a whole is small and its transection nearly circular in outline. The five segments of this region contain the neurone centers for the urinary bladder, the anus, some

of the musculature of the lower limbs, and the sensory reflexes of the perineum and genito-urinary organs.

Below the sacral region the spinal cord tapers rapidly (*conus medullaris*) and is continued downward for a considerable distance as the *filum terminale*. The fibrous membranes which surround the spinal cord continue even farther downward in the medullary canal to form the central ligament, which is finally attached to the sacrum or coccyx.

In the **lumbar region** there is a distinct enlargement,* chiefly involving the grey substance, which here includes the immense number of cells of the anterior horns whose "motor" fibres enter the large lumbar nerve trunks for the supply of the lower limbs.

* In those vertebrates which have no limbs—e. g., the reptiles—the cervical and lumbar enlargements are not found.

These nerve trunks also supply to the cord a great number of centripetal or sensory fibres which enter the dorsal and, later (through secondary neurones), the lateral columns; thus both of these columns are of large size in and above the lumbar region. The postero-internal column in this region attains an appreciable size, and a distinct pial septum marks its lateral boundary.



FIG. 378.—TRANSECTION OF THE SPINAL CORD OF A CHILD, FIFTH LUMBAR SEGMENT.

Weigert stain. $\times 7$.

The spinal cord is now nearly circular in trans-section, its ventrodorsal being perhaps slightly greater than its transverse diameter. The grey commissure lies very near the middle of the spinal cord, and the anterior median fissure is, therefore, quite as deep as the posterior median septum.

Both the ventral and dorsal grey horns are long and thick. Each dorsal horn contains a large area of gelatinous substance, is somewhat longer on its lateral than on its median side, and reaches nearly to the dorsal surface of the spinal cord, opposite the postero-lateral sulcus. The dorsal nerve roots entering at this level are *apparently* directed toward the middle of the tips of the dorsal horns of grey matter; once within the spinal cord they pass around to the median side of the dorsal horns.

The ventral horns, somewhat larger than the dorsal, present two short and broad protuberances, the one at the antero-mesial, and the other and more prominent at the antero-lateral angle. A similar though less prominent protuberance is seen at the base of the ventral horn, on its lateral aspect. Each of these projections contains a more or less well-defined group of motor nerve cells. The cell groups of the anterior horns in the lumbar region are therefore a *ventro-medial*, *ventro-lateral*, and *dorso-lateral*, together with an ill-defined central group occupying the deeper "intermediate zone" of grey matter.

The nerve centers contained in the lumbar region control the reflexes and musculature of the lower limbs and the lower part of the abdominal wall.

A transection of the spinal cord in the **thoracic region** is of small diameter, and is very nearly circular in outline. The white matter, since it contains the many nerve fibres going to and coming from the lumbar enlargement, is much more voluminous than the grey matter. The latter is reduced to a comparatively insignificant central mass.

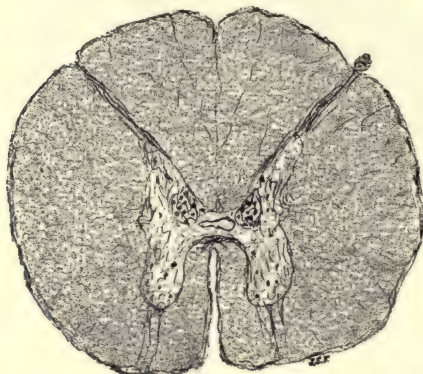


FIG. 379.—TRANSECTION OF THE SPINAL CORD OF A CHILD, EIGHTH THORACIC SEGMENT.

Weigert stain. $\times 7$.

The postero-internal column attains a considerable size in this region, and is distinctly marked off from the adjacent postero-lateral column by a fibrous septum derived from the pia mater. The posterior and the lateral columns, having been much augmented by the influx of fibres from the large posterior roots of the lumbar nerves, form the larger part

of the white matter. The grey matter consequently appears to be pushed forward, its grey commissure lies considerably ventral to the center of the spinal cord, the anterior median fissure is shorter than the posterior median septum, and the tips of the dorsal grey horns are far removed from the surface, being only connected with the postero-lateral sulcus by the slender dorsal nerve roots. In fact, the dorsal horns of grey matter in this region are reduced to a minimum size; they are short and slender and contain comparatively few nerve cells.

At the base of each dorsal horn, on its mesial side, there is a distinctly outlined cell group whose transection is of oval or circular outline. Indeed, this cell group, the *cell column of Clarke*, begins in the second or third lumbar segment, and is continued upward to the second or third thoracic—at times even into the lowermost cervical segments—at which level it has dwindled to a relatively insignificant group.*

The ventral grey horns are very short and narrow, and their cells can not be subdivided into groups as in the other regions of the spinal cord. In the upper part of the dorsal region a distinct

* In the lower lumbar region an ill-defined group of cells occupying a similar position and having the same function is known as the *nucleus of Stilling*.

protuberance makes its appearance at the base of the anterior horn, on its lateral aspect. This is the precursor of the larger *lateral horn* of the cervical region. In the upper dorsal region it contains a small cell group, the dorso-lateral.

The nerve centers of the dorsal segments control the upper abdominal region, the thorax, and the viscera.

In the **lower half of the cervical region** the spinal cord presents a distinct enlargement, within the grey matter of which are the nuclei for the upper limbs. The spinal cord in this region is somewhat flattened, its transverse diameter considerably exceeding its antero-posterior. The major portion of the white matter is still contained within its dorsal rather than its ventral portion, the grey commissure appearing to lie somewhat in front of the center. The posterior median septum dips inward for a much greater distance than does the anterior median fissure.

The posterior columns are decidedly larger than the anterior, and a distinct groove, from which a fibrous septum is continued



FIG. 380.—TRANSECTION OF THE SPINAL CORD OF A CHILD, SEVENTH CERVICAL SEGMENT.
Weigert stain. $\times 7$.

inward, separates the postero-internal from the postero-lateral column.

The dorsal grey horns are long, relatively slender, and more divergent than in the lower levels. They do not reach the surface of the spinal cord, but are connected therewith by the long, slender dorsal nerve roots. The grey matter of the dorsal horns in this region is more or less invaded by bundles of nerve fibres derived from the lateral and posterior columns; the tips of the

dorsal horns are thus almost cut off from the deeper portions of grey matter.

The ventral horns are both long and broad. They present three noticeable promontories or processes—a ventral (ventro-medial), a medial (ventro-lateral), and a lateral. The lateral, because of its special prominence, is frequently called the *lateral horn*; it is one of the noticeable characteristics of the cervical region.

Each of these processes contains a corresponding cell group; hence we distinguish in the cervical enlargement a *mesial*, a *ventral*, and a *lateral* group, together with a small *intermedio-lateral*, which is partially or completely detached from the dorsal portion of the lateral group. There is also a small disseminated *central group* of nerve cells occupying the deeper portion of the anterior horn.

The nuclei of the segments included in the cervical enlargement contain the centers for the musculature and sensory reflexes of the upper limbs. The partial control of the pupillary movements in the eye is also located in the lowermost segments of this region.

In the **upper half of the cervical region** a transection of the spinal cord, except for its larger size, resembles very closely that



FIG. 381.—TRANSECTION OF THE SPINAL CORD OF A CHILD,
FOURTH CERVICAL SEGMENT.

Weigert stain. $\times 7$.

of the thoracic region. The larger size is due to an increase in the white matter of the posterior and lateral columns, consequent upon the acquisition of new fibres which enter the subjacent segments from the nerves supplying the upper extremities, together with an

increased number of centrifugal fibres from the cerebrum which are distributed to the grey matter of this region.

The anterior columns are also much increased in size by the

addition of many fibres coming down from the medulla and cerebellum, which place the nerve centers of the spinal cord in close relation with those of the cranial nerves and with the association centers of the cerebellum.

In addition to the large size of its white columns, a noticeable characteristic of the upper cervical region is the prominence of its lateral horns of grey matter. Just dorsal to the lateral horns is also a peculiar *reticular formation* which results from an invasion of the adjacent portions of the lateral white columns by bands of grey matter. The grey matter thus forms a coarse network whose meshes inclose isolated bundles of longitudinal nerve fibres.

The ventral horn cells of this region are scarcely divisible into groups, but a large and distinct cell group, the *intermedio-lateral cell column*, occupies the so-called lateral horn.

The nuclei of the upper cervical region enervate the skin and muscles of the neck and shoulder, they also supply the diaphragm. The nerve cells of this region not only supply the cervical spinal nerves, but they also send root bundles to the spinal accessory or eleventh cranial nerve.

THE MEDULLA OBLONGATA AND BRAIN STEM.—Passing from the first cervical segment of the spinal cord to the lower portion of the medulla, a remarkable rearrangement of the central grey mass is noticed, the change being apparently dependent upon three prime factors, as follows:

1. The passage of numerous bundles of white fibres between the lateral columns of the spinal cord and the anterior columns or pyramids of the medulla, cuts off the ventral horns of the grey matter; the detached ventro-lateral portion with its lateral cell groups is thus displaced lateralward, while the base of the ventral horns with their mesial cell groups remain adherent to the grey commissure near the region of the central canal. Between these two portions of the ventral horns is an irregularly disposed and interlacing mass of nerve fibres, interspersed with fragments of grey matter, which forms the *formatio reticularis* of the medulla oblongata.

2. The anterior median fissure in this region becomes merely a shallow and deep raphé across which many nerve fibres decussate. Those long fibre bundles which in the spinal cord occupied the lateral and posterior columns are now found in the anterior or ventral portion (pyramids, *formatio reticularis*, and fillet) of the medulla oblongata.

3. The posterior median septum rapidly becomes a deep sulcus which soon broadens out to form the fourth ventricle, thus pushing the diminished remains of the posterior columns, with the adjacent dorsal horns, farther and farther lateral and ventralward until the dorsal horns finally come to occupy a position in which their long axis is directed, from the grey commissure, lateralward and but slightly dorsalward.

The fibre paths of the posterior columns, consisting now of secondary neurones, having crossed, almost in a body, to the fillet of the opposite side in the ventral portion of the medulla, uncovers the dorso-mesial surface of the dorsal grey horns, leaving them exposed in the floor of the fourth ventricle, which is formed by the much expanded central canal and posterior median fissure. It will thus be seen that the nuclei of the centripetal cranial nerve fibres (sensory nuclei), whose homologues in the spinal cord were found in the dorsal horns, in the medulla oblongata are to be found in the floor of the fourth ventricle, the grey matter which forms this region being both homologous, and nearly continuous, with the dorsal horns of the spinal cord.

The nuclei of the centripetal paths (motor nuclei), which in the spinal cord included the various cell groups of the ventral horns, are found in the medulla oblongata in two regions: first, a median group near the anterior median raphé, which, in the lower levels of the medulla oblongata, lies just ventro-lateral to the central canal and grey commissure, but higher in the medulla is found on either side of the median line beneath the floor of the fourth ventricle, from which it is separated by a layer of grey matter continued upward from the grey commissure of the spinal cord; and second, a lateral group representing the detached tips of the ventral horns, which is now found well toward the lateral surface of the medulla oblongata, and which in the lower part of the medulla forms the lateral nucleus, but higher up becomes the nucleus ambiguus of the ninth and tenth cranial nerves.

The laterally displaced dorsal horns are now separated from the detached portions of the ventral by an insignificant column of white fibres, the upward continuation of the lateral columns of the spinal cord.

It will later be shown that the motor fibres of the twelfth, sixth, fourth, and third cranial nerves take their origin from the medial group of nuclei, while the motor portions of the tenth, ninth, seventh, and fifth nerves arise from the lateral group. The

respectively terminate. The central neurones, whose cell bodies form these nuclei, send their neuraxes ventralward and toward the anterior median raphé, which they cross to the opposite side, and enter the tract of the *mesial fillet* (*mesial lemniscus, laqueus*). Thus it is that the posterior columns of the spinal cord disappear in the medulla, and the dorsal horns of grey matter are in this way brought into direct relation with the layer of ependymal cells which lines the floor of the fourth ventricle.

The Inferior Olivary Body.—Another and still larger isolated grey nucleus, beginning at a slightly higher level than the above and extending farther cephalad, is the inferior olivary body. This nucleus is inserted between the ventrally situated pyramids on the one hand, and the lateral columns, lateral nucleus, and *formatio reticularis* on the other. The inferior olivary body is a large ovoid mass with a central core of white fibres and a crinkled shell of grey matter; its convoluted surface presents a ribbon-like appearance when seen in transection. The olivary nucleus extends from near the spinal border of the medulla oblongata upward to the lower portion of the pons Varolii.

The white matter of the medulla oblongata presents two prominent decussations of long fibre tracts, which have already been mentioned as cutting off the lateral from the medial cell groups of the ventral horns. The more spinalward of these is the motor decussation, the more cephalad is the great sensory decussation of the mesial fillet.

The motor decussation occurs at the junction of the first cervical segment and spinal border of the medulla oblongata; it is found at the level of the lower portions of the nuclei of Goll and Burdach. The greater portion of the nerve fibres composing the pyramids of the medulla decussate through the median raphé at this level, and pass obliquely downward to the opposite lateral column of the spinal cord.

The sensory decussation occurs at a slightly higher level, its fibres chiefly coming from the nuclei of Goll and Burdach, to pass cephalad in an obliquely ventro-mesial direction, piercing the median raphé just dorsal to and a little above the motor decussation. Having reached the opposite side they immediately turn cephalward to form the mesial fillet, a large flattened bundle of longitudinal white fibres lying next the median raphé and just dorsal to the pyramidal tracts. The interlacing of these fibres as they approach the raphé forms a reticular mass of white matter which

is distinguished from the more lateral *grey reticular formation* (*formatio reticularis grisea*); in contradistinction this is known as *the white reticular formation* (*formatio reticularis alba*).

At the mid-level of the medulla oblongata a small portion of the lateral column moves obliquely dorsalward to enter the cere-

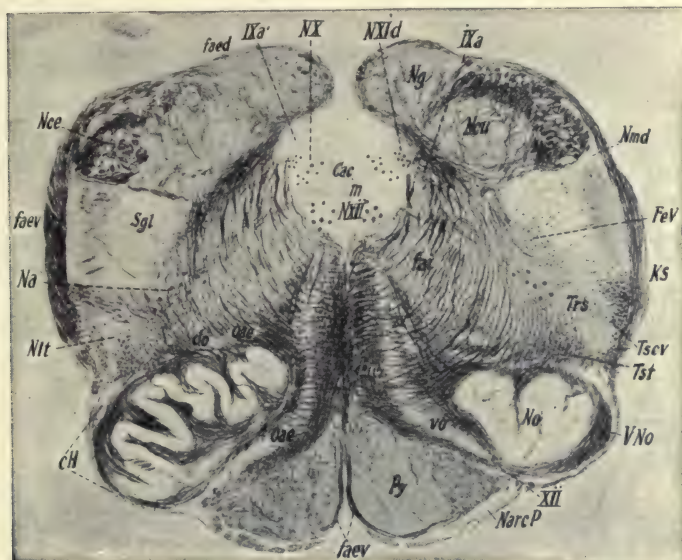


FIG. 383.—TRANSECTION OF THE HUMAN MEDULLA OBLONGATA AT THE LEVEL OF THE LOWER MARGIN OF THE INFERIOR OLIVARY BODY.

Cac, central canal; *cH*, central tract of the tegmentum; *do*, dorso-olivary fibres; *faed*, the dorsal external arcuate fibres; *faev*, the ventral external arcuate fibres; *fai*, the internal arcuate fibres; *FeV*, accompanying tracts of the trigeminus; *IXa*, spinal root of the glossopharyngeus; *IXa'*, accessory bundle of the same; *KS*, direct cerebellar tract; *Lm*, mesial lemniscus; *Na*, nucleus ambiguus; *NarcP*, arcuate nucleus of the pyramids; *Nce*, external nucleus of Burdach; *Neu*, nucleus of Burdach; *Ng*, nucleus of Goll; *Nlt*, nucleus of the lateral column; *Nmd*, dorso-marginal nucleus of Ziehen; *No*, inferior olive; *NX*, dorsal vago-glossopharyngeal nucleus; *NXId*, dorsal spinal accessory nucleus; *NXII*, hypoglossal nucleus; *Oae*, accessory olivary nuclei; *Py*, pyramids; *Sgl*, gelatinous substance of Rolando; *Trs*, rubro-spinal tract (Monakow's bundle); *Tscv*, antero-lateral ascending tract of Gowers; *Tst*, spino-tectal and thalamic tract; *VNo*, olivary capsule; *vo*, ventro-olivary fibres; *XII*, hypoglossal nerve. Weigert's stain. $\times 5$. (After Marburg.)

bellum. These fibres are reinforced by a considerable bundle coming from the cerebellum to enter the inferior olivary body. Together these bundles form a projecting column of white matter in close relation to the substantia gelatinosa of Rolando in the tips of the dorsal grey horns; this mixed tract is the *restiform body*

or *inferior peduncle of the cerebellum*. At the mid-level of the medulla the gelatinous substance of Rolando is so increased in amount as to form a slight protuberance, tubercle of Rolando, which is seen on the ventral border of the restiform body.

The Nucleus of the Twelfth Cranial Nerve.—The four lower cranial nerves are given off from this portion of the rhombencephalon. The twelfth, a motor nerve, arises from a grey nucleus on either side of the raphé just ventral to the grey commissure. Its nucleus extends from a point just above the motor decussation upward to the level of the caudal margin of the pons Varolii. Fibres pass ventralward from this nucleus and emerge from the medulla oblongata through a groove between the pyramid and the olivary body.

The eleventh cranial nerve (motor) arises from the intermediolateral cell group in the ventral horns of the six upper cervical segments and from the lateral nucleus of the medulla. Fibres pass from these nuclei through the lateral columns, from which they make their exit, and passing upward unite with each other to form the trunk of the spinal accessory.

The tenth cranial nerve arises in two main divisions, the motor and the sensory. The motor portion takes its origin from the nucleus ambiguus which, toward the spinal cord, is continuous with the lateral nucleus and the ventral horns. Higher in the medulla the *nucleus ambiguus* also gives origin to the peripheral neurones of the ninth nerve. The motor fibres of the tenth and ninth nerves make their exit from the lateral surface of the medulla oblongata, ventral to the restiform body.

The sensory roots of these nerves enter the medulla in company with the outgoing motor fibres; they pass to a triangular area of grey matter in the floor of the fourth ventricle. This is the *chief nucleus* of the vagus. It is continuous above with the similar nucleus of the ninth nerve.

Descending branches from the fibres of the ninth and tenth nerves form a small but prominent tract which lies in the margin of the grey matter, and ventro-lateral from the chief nuclei of these nerves. This is the *tractus solitarius* or *spinal root of the ninth and tenth nerves*. It is continued downward as far as the cervical region, and its path is surrounded by a thin shell of grey matter (*nucleus of the tractus solitarius*) in which its fibres terminate.

The ninth or glossopharyngeal nerve is very similar to the tenth in its origin and its exit from the medulla. The root bundles

of the tenth nerve, however, are rather coarser and form larger bundles than those of the ninth.

At the level of the ninth nerve the *dorsal and medial accessory olivary nuclei* make their appearance. They form, on either side, two isolated flattened grey masses. The dorsal accessory nucleus is flattened antero-posteriorly, and lies just behind the mesial half

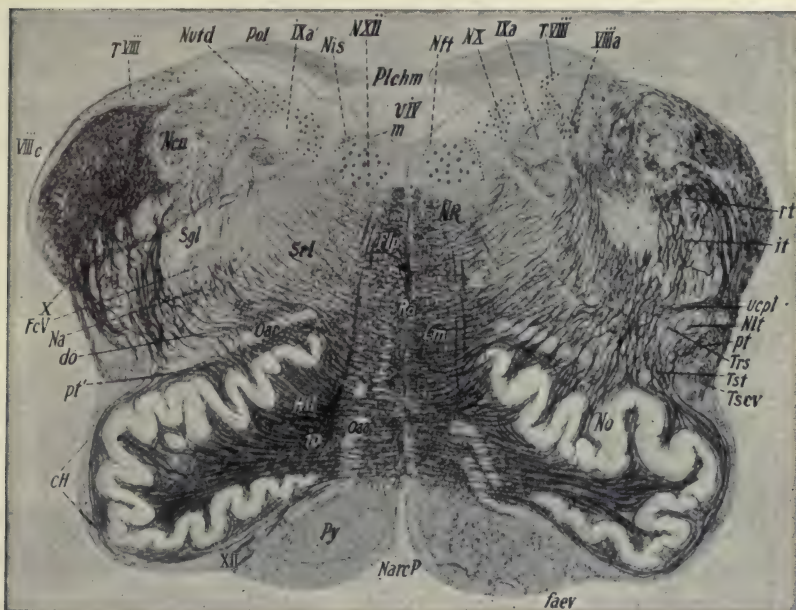


FIG. 384.—TRANSECTION OF THE HUMAN MEDULLA OBLONGATA AT THE MID-LEVEL OF THE INFERIOR OLIVARY BODIES.

cH, central tract of the tegmentum; *do*, dorso-olivary fibres; *faev*, ventral external arcuate fibres; *FeV*, accompanying tracts of the trigeminus; *Flp*, posterior longitudinal bundle; *Hil*, hilum of the olivary body; *io*, intraolivary fibres; *it*, arcuate trigeminal fibres; *IXa*, spinal root of the glossopharyngeus; *IXa'*, accessory bundle of same; *Lm*, mesial lemniscus; *m*, dorsal longitudinal bundle of Schütz; *Na*, nucleus ambiguus; *NarcP*, arcuate nucleus of the pyramids; *Ncu*, nucleus of Burdach; *Nft*, nucleus of the eminentia teres; *Nis*, intercalate nucleus of Staderini; *NH*, nucleus of the lateral column; *No*, inferior olivary body; *NR*, nucleus of Roller; *Ntd*, chief nucleus of the vestibular nerve; *NX*, dorsal or chief nucleus of the vagus; *NXII*, hypoglossal nucleus; *Oaa*, mesial, and *Oae*, dorsal accessory olivary nuclei; *Plchm*, mesial choroid plexus; *Pol*, ponticulus; *pt*, trigeminal arcuate fibres; *pt'*, marginal trigeminal arcuate fibres; *Py*, pyramids; *Ra*, raphé; *rt*, retrogeminal arcuate fibres; *Sgl*, gelatinous substance of Rolando; *Srl*, lateral reticular substance; *Trs*, rubro-spinal tract of von Monakow; *Tsev*, Gowers' tract; *Tst*, spino-tectal and thalamic tract; *TVIII*, acoustic tubercle; *vcpl*, ventral collateral plexus; *VIIIa*, spinal root of the auditory nerve; *VIIIc*, cochlear nerve; *VIV*, the fourth ventricle; *X*, vagus nerve; *XII*, hypoglossal nerve. Weigert's stain. $\times 5$. (After Marburg.)

of the inferior olivary body. The mesial accessory olivary nucleus is transversely flattened, and lies between the mesial surface of the olivary body and the median raphe.

Just below the spinal border of the pons Varolii the anterior pyramids present a thin layer of grey matter on their ventral surface; this is the *arcuate nucleus* (nucleus of the external arcuate fibres, *nucleus arcuatus*).

Opposite the upper end of the chief glossopharyngeal nucleus the medulla comes into relation ventrally with the pons Varolii, but is covered dorsally by the overhanging cerebellum. At the lower border of the pons Varolii the eighth, seventh, and sixth cranial nerves are given off, the sixth from the groove between the pyramid and the cephalic end of the inferior olivary body, the seventh lateral to the olivary body, and the eighth still farther lateral and somewhat dorsal from the seventh.

The twelfth, sixth, and later the third cranial nerves may be collectively considered as a ventral group which are given off in a ventral plane near the median line; the eleventh, tenth, ninth, eighth, seventh, and fifth form a lateral group, having their superficial origin from the lateral surface of the nervous system and in nearly the same vertical plane. The fourth nerve, since it makes its exit from the dorsal surface, is without a homologue. The second and first cranial nerves are for many reasons considered as diminutive lobes of the cerebrum itself, and as such are not homologous with the other cranial nerves.

THE PONS VAROLII

The pons Varolii or metencephalon occupies a region corresponding to the upper half of the fourth ventricle. The lateral walls of the ventricle approach each other in this region, finally uniting in the median line and thus surrounding a central canal, the aqueduct of Sylvius, which extends cephalward through the mesencephalon to the third ventricle. These cavities are not only homologous, but at the spinal end of the fourth ventricle are also continuous with the central canal of the spinal cord.

In the metencephalon the morphological structures of the medulla oblongata or myelencephalon are continued upward in the dorsal half of the organ, known as its *tegmentum*, with the single exception of the pyramids, which, as longitudinally disposed fibre bundles, enter the ventral portion to interlace with the transverse fibre bundles of the pons Varolii. This reticular mass of nerve

fibres forms the ventral portion or *crusta* of the pons. Since the transverse fibres of the pons Varolii pass directly into the cerebellum, these fibres may be considered as forming the *middle peduncles* of this organ.

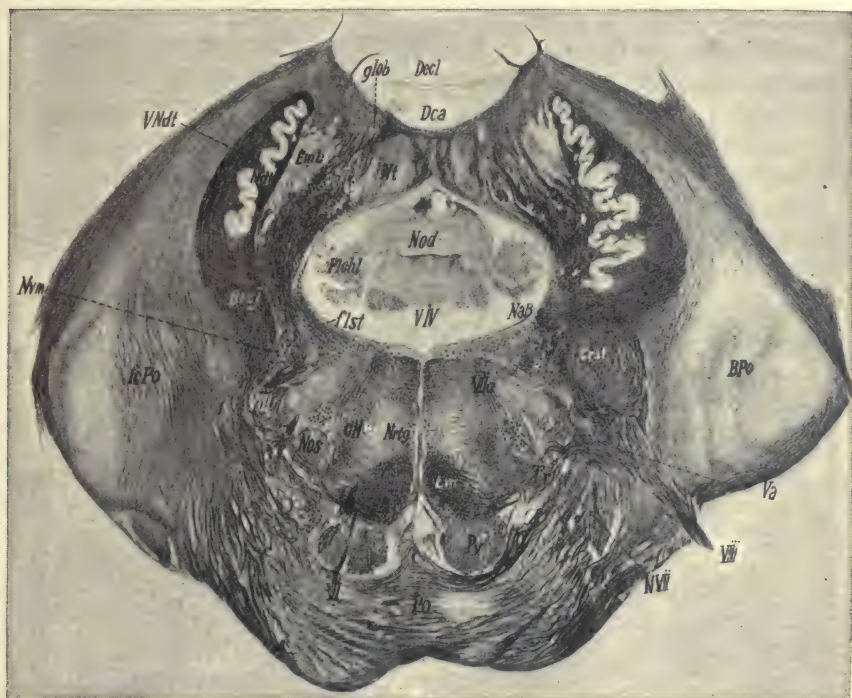


FIG. 385.—A SECTION THROUGH THE LOWER BORDER OF THE PONS VAROLII OF THE HUMAN BRAIN.

Brj, brachium conjunctivum; *BPo*, middle peduncle of the cerebellum; *cH*, central tract of the tegmentum; *Crst*, restiform body; *Decl*, declive; *Dca*, anterior cerebellar commissure; *Emb*, nucleus emboliformis; *fcPo*, cerebello-pontine fibres; *flst*, peduncle of the flocculus; *glob*, globular nucleus; *Lm*, mesial lemniscus; *NaB*, von Bechterew's nucleus; *Ndt*, dentate nucleus of the cerebellum; *Nod*, nodulus cerebelli; *Nos*, superior olivary nucleus; *Nt*, nucleus tecti; *NVII*, facial nucleus; *Nvm*, motor nucleus of the trigeminus; *Nrtg*, reticular nucleus of the tegmentum; *Plehl*, lateral choroid plexus; *Po*, pons Varolii; *Py*, pyramid; *Tr*, trapezoid body; *Va*, bundle of Vieq d'Azyr; *VI*, abducens nerve; *VIIa*, first portion of the root of the facial nerve; *VIII*, auditory nerve; *VIV*, fourth ventricle; *VNdt*, capsule of the dentate nucleus. Weigert's stain. $\times 28$. (After Marburg.)

In addition to those structures which are continued upward from the medulla oblongata, the metencephalon contains the central paths and nuclei of those cranial nerves which enter this region.

Thus the floor of the fourth ventricle in its upper half contains that dorsal grey matter which is continued upward from the chief nuclei of the ninth and tenth nerves; it is thus homologous with the dorsal horns of the spinal cord. This grey mass at the lower border of the pons forms the *chief or mesial nucleus of the eighth cranial nerve*.

Just ventral to this nucleus is an ovoid compact group of large motor nerve cells, the *nucleus of the sixth or abducens nerve*. The nuclei of the sixth pair are thus in the same vertical plane as those of the twelfth, but are somewhat more separated from one another by a median longitudinal fibre bundle, the *medial or posterior longitudinal fasciculus*, which, in its upward course, curves dorsalward in the medulla oblongata, so that in the pons Varolii it lies on either side of the median raphé and beneath the grey matter of the floor of the fourth ventricle.

The deeper part of the pontal tegmentum contains a continuation of the formatio reticularis of the medulla. Ventral to this and separating it from the pons fibres are the longitudinal fibre bundles of the mesial fillet, which in transection form an oval bundle with its long axis at nearly a right angle to the median raphé.

Lateral to the formatio reticularis and above, but in the same vertical plane as the inferior olivary body, is the *superior olivary nucleus*, a small oval mass of grey matter which forms a cell station in the path of the cochlear division of the auditory nerve. In some of the lower mammals this nucleus is more highly developed than in man. Connecting the superior olivary body with a similar region of the opposite side is a transverse bundle of fibres, the *trapezoid body*, which crosses the pons just ventral to the mesial fillet, but dorsal to the pyramidal tracts and transverse fibres of the pons Varolii.

In close proximity to the superior olivary nucleus, on its dorso-lateral side, is the *nucleus of the seventh cranial nerve*, a slender rounded cell column whose position is above but homologous with that of the nucleus ambiguus, the lateral nucleus, and the ventral horns of the spinal cord.

The *eighth cranial nerve* enters just lateral to the nucleus of the seventh, its vestibular division lying at a somewhat lower level than its cochlear portion. The vestibular nerve near its point of entrance is surrounded by a ganglionic mass of grey matter which lies in the extreme lateral portion of the metencephalon. This

nucleus, being penetrated by the cochlear nerve, is thus divided into two portions, a *ventral* or *accessory nucleus*, and a *dorsal nucleus* or *tuberculum acusticum*. Between the cochlear nuclei

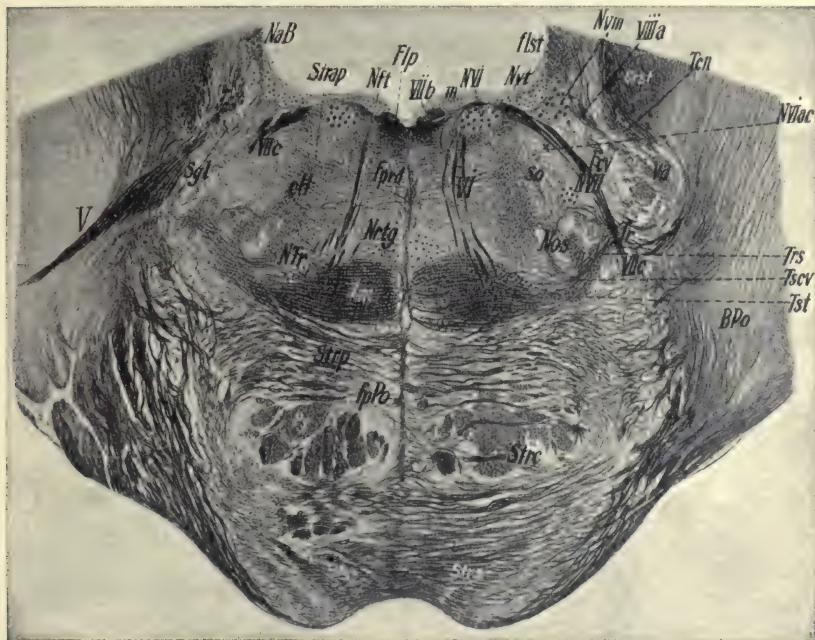


FIG. 386.—A SECTION THROUGH THE MIDDLE OF THE HUMAN PONS VAROLII.

BPo, middle cerebellar peduncle; *cH*, central tract of the tegmentum; *Crst*, restiform body; *FeV*, the accompanying tracts of the trigeminus; *Ftp*, posterior longitudinal bundle; *flst*, peduncle of the flocculus; *fpPo*, longitudinal pontine fibres; *fprd*, predorsal bundle; *Lm*, mesial lemniscus; *m*, dorsal longitudinal bundle of Schütz; *NaB*, nucleus of von Bechterew; *Nft*, nucleus of the eminentia teres; *Nrtg*, reticular nucleus of the tegmentum; *NTr*, trapezoid nucleus; *NVI*, abducens nucleus; *NVIac*, accessory nucleus of the abducens; *NVII*, facial nucleus; *Nvm*, motor nucleus of the trigeminus; *Net*, triangular or chief nucleus of the vestibular nerve; *Py*, pyramid; *Sgl*, gelatinous substance of Rolando; *so*, peduncle of the superior olive; *Strap*, strie acusticæ; *Strc*, middle, *Strp*, deep, and *Strs*, superficial layer of the pons; *Tcn*, nucleo-cerebellar tract; *Tr*, trapezoid body; *Trs*, rubro-spinal tract of von Monakow; *Tso*, Gowers' tract; *Tst*, spino-tectal and thalamic tract; *V*, trigeminus; *va*, bundle of Vieq d'Azyr; *VI*, abducens; *VIIb*, second, and *VIIIc*, third portion of the facial root; *VIIIa*, spinal vestibular root. Weigert's stain. $\times 34$. (After Marburg.)

and the ventro-lateral wall of the fourth ventricle the grey matter of the formatio reticularis appears to be directly continued latero-alward into the substance of the cerebellum.

Just at this point is a disseminated group of very large nerve

cells, *Deiters' nucleus*. Still more lateral and just at the margin of the central grey matter of the cerebellum, is the small-celled nucleus of *von Bechterew*. These two nuclei, together with the

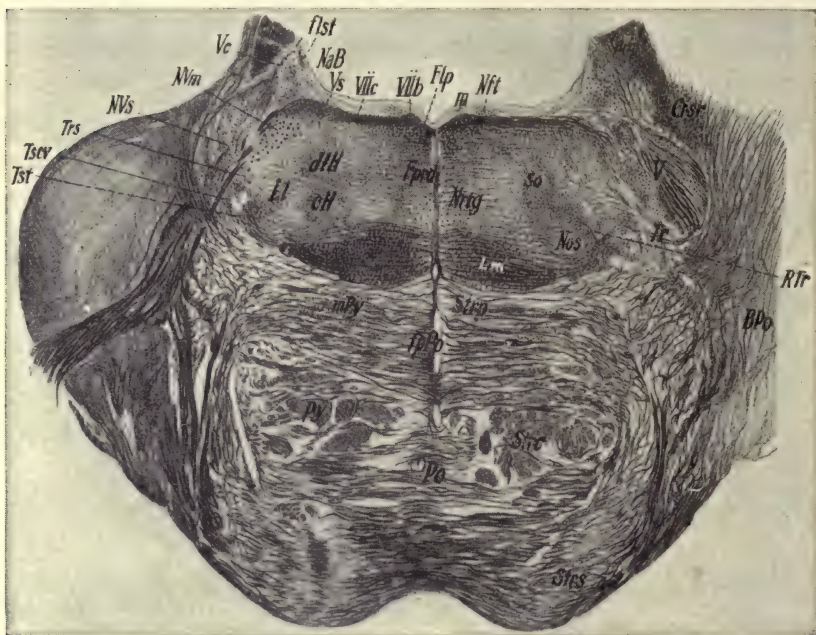


FIG. 387.—A SECTION OF THE HUMAN PONS VAROLII AT THE LEVEL OF THE TRIGEMINUS NERVE.

BPo, middle cerebellar peduncle; *cH*, central tract of the tegmentum; *dlH*, dorso-lateral tract of the tegmentum; *Flp*, posterior longitudinal bundle; *flst*, peduncle of the flocculus; *fpPo*, longitudinal pontine fibres; *Fprd*, predorsal fasciculus; *Ll*, lateral lemniscus; *Lm*, mesial lemniscus; *m*, dorsal longitudinal bundle of Schütz; *mPy*, cortico-pontine tract; *NaB*, nucleus of von Bechterew; *Nft*, nucleus of the eminentia teres; *Nos*, superior olivary nucleus; *Nrtg*, reticular nucleus of the tegmentum; *NVm*, motor trigeminal nucleus; *NVs*, sensory trigeminal nucleus; *Po*, pons; *RTTr*, radial fibres of the trapezoid body; *So*, peduncle of the superior olive; *Strc*, middle layer of the pons; *Strp*, deep layer of the pons; *Strs*, superficial layer of the pons; *Tr*, trapezoid body; *Trs*, rubro-spinal tract; *Tscv*, Gowers' bundle; *Tst*, spino-tectal and thalamic tract; *V*, trigeminus; *Vc*, cerebral root of the trigeminus; *VIIb*, second portion of the facial root; *VIIc*, third portion of same; *Vs*, crossed root of the trigeminus. Weigert's stain. $\times 34$. (After Marburg.)

chief or mesial auditory nucleus, are connected with the path of the vestibular nerve.

In the lateral wall of the fourth ventricle is a transversely flattened oval bundle of nerve fibres, which arises from the central grey matter of the cerebellum and passes, as the *brachium con-*

junctivum or *superior peduncle of the cerebellum*, in a convergent cephalad course, at the same time approaching the median line to decussate in the mesencephalon with its fellow of the opposite side. On the ventro-mesial aspect of the superior peduncle, near its origin, is the superior end of the restiform body or inferior peduncle of the cerebellum, which here approaches its termination in the *vermis cerebelli*.

The roof of the fourth ventricle at this level is formed by the *vermis of the cerebellum*. On its ventral surface and near the median line is a small group of cells, the *nucleus fastigijs*. Dorsal to this nucleus are the convolutions of the superior *vermis*, while farther lateral is the *dentate nucleus* of the cerebellum, in section a ribbon-like mass of grey matter whose general appearance closely simulates that of the inferior olivary body. The dentate nucleus is embedded within the central white matter of the cerebellum.

At the mid-level of the pons Varolii the fifth nerve penetrates the organ from its lateral surface and passes inward to the tegmentum. On the ventro-mesial side of the trigeminal fibres is its chief motor nucleus, a small group of motor cells; on its dorso-lateral side is the larger, triangular, sensory nucleus of the trigeminus, whose apex extends downward through the pons, and beyond which the spinal root of the fifth nerve is continued into the medulla oblongata.

In the upper part of the pons the superior cerebellar peduncles have passed to a more ventral plane, and now lie in the lateral wall of the much narrowed fourth ventricle. Mesial to the peduncles, in relation to the ventro-lateral angle of the ventricle, is a small bundle of scattered nerve fibres, the descending cerebral root of the fifth nerve. The ventral margin of the grey matter on the inner side of this root contains a group of pigmented nerve cells which, as the *substantia ferruginea* or *locus cæruleus*, extends cerebralward into the midbrain.

The central portion of the pontal tegmentum in its upper part still consists of the *formatio reticularis*, which is continued upward through the isthmus rhombencephali and midbrain.

THE MESENCEPHALON

Entering the mesencephalon, at the isthmus rhombencephali, the *decussation of the fourth nerve* can be seen forming the roof of the *aqueduct of Sylvius*, which canal represents the cephalic continuation of the fourth ventricle and occupies the axis of the

organ; it is therefore homologous with the central canal of the spinal cord. At a slightly higher level, lateral to the grey matter

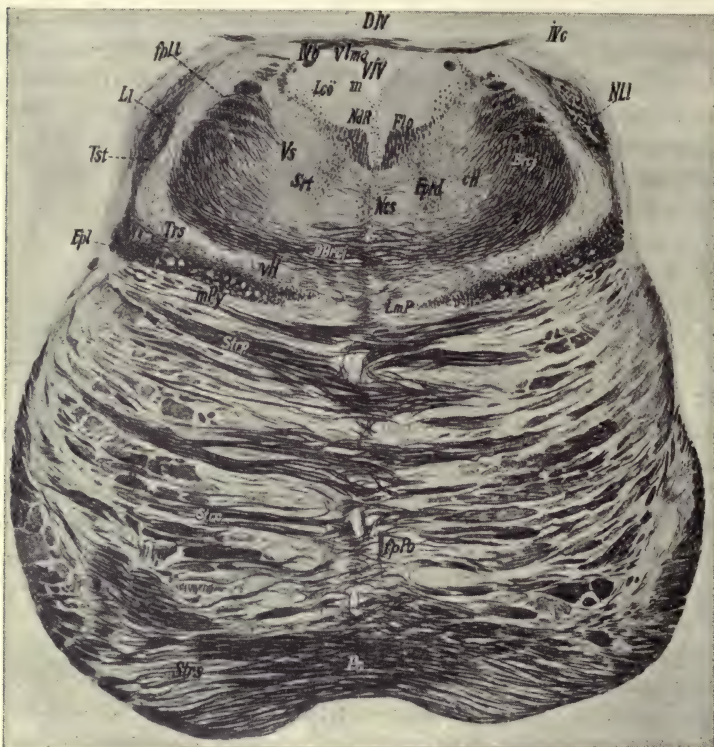


FIG. 388.—A SECTION OF THE HUMAN BRAIN STEM AT THE LEVEL OF THE CEREBRAL BORDER OF THE PONS VAROLII.

Brcj, brachium conjunctivum; *cH*, central tract of the tegmentum; *DBrcj*, decussation of the brachium conjunctivum; *DIV*, decussation of the trochlearis nerve; *Fpl*, lateral pontine bundle; *Fip*, posterior longitudinal fasciculus; *fpLl*, perforating fibres of the lateral lemniscus; *fpPo*, longitudinal pontine fibres; *Fprd*, predorsal bundle; *IVb*, descending root, and *IVc*, point of exit of the trochlearis nerve; *Lco*, locus coeruleus; *Ll*, lateral lemniscus; *Lm*, mesial lemniscus; *LmP*, bundle from the fillet to the crusta; *m*, dorsal longitudinal fasciculus of Schütz; *mPy*, cortico-pontine tract; *Ncs*, superior central nucleus; *NdR*, dorsal nucleus of the raphe; *NLL*, nucleus of the lateral lemniscus; *Po*, pons; *Srt*, substantia reticularis alba; *Strc*, middle, *Strp*, deep, and *Strs*, superficial layers of the pons; *Trs*, rubro-spinal tract; *Tst*, spino-tectal and thalamic tract; *vH*, ventral field of the tegmentum; *VIF*, fourth ventricle; *Vlma*, anterior medullary velum; *Vs*, crossed root of the trigeminus. Weigert's stain. $\times 3$. (After Marburg.)

surrounding the aqueduct and lying just mesial to the cerebral root of the fifth nerve, is a small circular bundle of coarse nerve fibres, the *cerebral* or *descending root of the fourth cranial nerve*.

The lateral and mesial fillets, superior cerebellar peduncles, pyramidal tracts, and posterior longitudinal fasciculi are continued upward through the mesencephalon. The mesial fillet lies rather more lateral from the median raphé than in the lower levels, and its outer border is blended with the *lateral fillet*. The superior cerebellar peduncles approach the median line and soon decussate. This decussation occurs in the cephalic end of the midbrain. The pyramidal tracts form the large bundle of longitudinal fibres which compose the columns of the *cruræ cerebri*. The fibres of the posterior longitudinal fasciculus on either side of the median line, form a deep longitudinal trough in which rests the grey matter which incloses the aqueduct of Sylvius. In this grey matter several groups of large motor cells mark the beginning of the *nuclei of the third pair of cranial nerves*. These nuclei extend cephalad for a considerable distance. The *nuclei of the fourth cranial nerves* form, on either side, a group of large pigmented cells which indent the dorsal margin of the posterior longitudinal fasciculus.

Opposite the anterior corpora quadrigemina the third nerve makes its exit. At this level the grey matter, which was continued upward from the medulla oblongata and dorsal half of the pons Varolii, is reduced to a comparatively thin cylindrical mass which surrounds the aqueduct of Sylvius. The *nucleus of the third cranial nerve*, which is embedded in this grey matter, presents a median and a lateral cell group. The *median nucleus* lies in the median line, in the angle of the trough formed by the posterior longitudinal fasciculi; the *lateral nucleus* indents the dorsal surface of these bundles.

In the ventral portion of the organ at this level, and on either side of the median line, is a large oval reddish-grey mass of nerve cells, the *red nucleus (nucleus ruber)*. This nucleus occurs at the level of the decussation of the superior cerebellar peduncles, and in it the fibres of these tracts terminate immediately after their decussation.

Ventral to the red nucleus, but separated from it by a dark mass of nerve cells, the *substantia nigra* of Sömmerring, is the free portion of the crus cerebri, which contains the continuation of the pyramidal tracts.

The *optic tracts* at this level pass dorsalward around the lateral surface of the mesencephalon to reach the medial geniculate bodies in the angle between the optic thalamus and the brain stem.

Above the border of the pons Varolii the *crura cerebri* diverge,

leaving a deep but broad sulcus in the median line, in the floor of which is the *posterior perforated space*. The root bundles of the third cranial nerves pass ventralward from their nuclei of

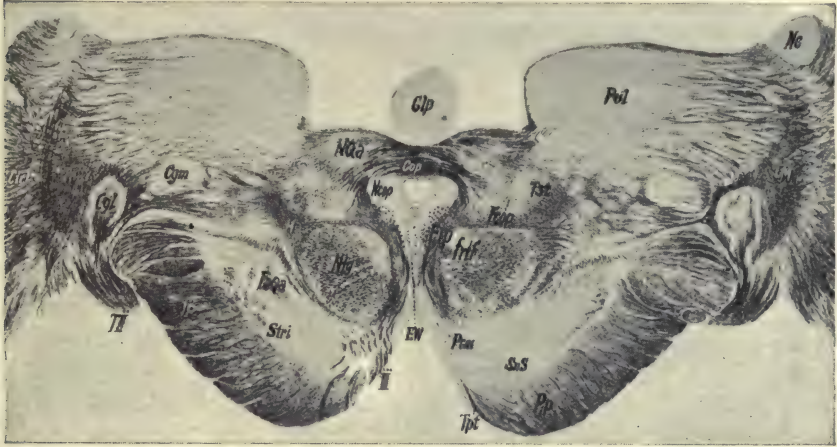


FIG. 390.—A SECTION OF THE HUMAN BRAIN STEM, AT THE LEVEL OF THE POSTERIOR BORDER OF THE RED NUCLEUS.

Cgl, lateral geniculate body; *Cgm*, mesial geniculate body; *Cirl*, internal capsule; *Cop*, posterior commissure; *EW*, Edinger-Westphal nucleus; *FeQa*, efferent fibres from the roof of the mesencephalon; *Ftp*, posterior longitudinal bundle; *fp*, perforating fibres of the crura; *frtf*, fasciculus retroflexus of Meynert; *Glp*, pineal gland; *H*, Forel's field; *III*, oculomotor nerve; *LM*, Wernicke's field; *Ne*, caudate nucleus; *Ncp*, nucleus of the posterior commissure; *Nqa*, nucleus of the superior corpora quadrigemina; *Nig*, red nucleus; *Pm*, peduncle of the mammillary body; *Pp*, crura; *Pul*, pulvinar; *S.S*, substantia nigra; *Stri*, intermediate layer; *III*, optic tract; *Tpt*, transverse tract of the peduncle; *Tst*, spino-tectal and thalamic tract. Weigert's stain. $\times 1\frac{1}{2}$. (After Marburg.)

origin, penetrate the region of the red nuclei, and emerge through the posterior perforated space at the mesial border of the crura cerebri.

THE DIENCEPHALON.—With the next step cerebralward the aqueduct of Sylvius opens into the third ventricle and the mesencephalic nuclei are replaced by the large basal nuclei of the cerebrum. This group of nuclei include the optic thalamus, caudate nucleus, lenticular nucleus, hypothalamic nucleus, and the nucleus of the posterior longitudinal fasciculus (Darkschewitsch's nucleus).

The *nucleus of the posterior longitudinal fasciculus* (*Darkschewitsch*) lies on either side of the median line, ventral and somewhat cephalad from the oculo-motor nuclei. In it the posterior longitudinal fasciculus, in part, at least, terminates.

On either side of the third ventricle, dorso-lateral from the red nucleus, is the large ovoid group of nuclei which collectively form the *optic thalamus*. The group of thalamic nuclei include the

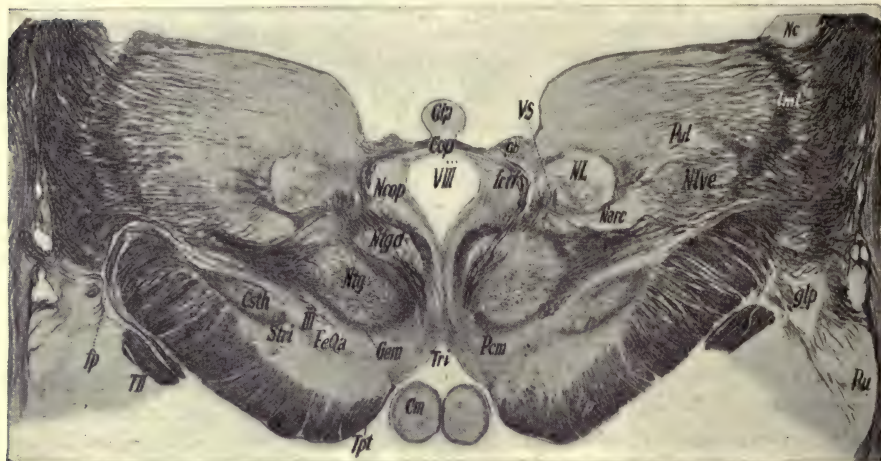


FIG. 391.—A SECTION OF THE HUMAN BRAIN STEM, AT THE MID-LEVEL OF THE RED NUCLEUS.

Cm, mamillary body; *Ccp*, posterior commissure; *Csth*, subthalamic body of Luys; *FeQa*, efferent fibres from the roof of the mesencephalon; *fp*, perforating fibres of the crura; *frtf*, Meynert's bundle; *Gem*, ectomammillary ganglion; *Gb*, ganglion habenulae; *Glp*, pineal gland; *glp*, globus pallidus; *III*, oculomotor nerve; *lml*, lateral medullary layer of the thalamus; *Narc*, arcuate nucleus of the thalamus; *Nc*, caudate nucleus; *Ncop*, nucleus of the posterior commissure; *Nl*, centre median of Luys; *Nlve*, external latero-ventral nucleus of the thalamus; *Ntd*, dorsal portion of same; *Ntg*, red nucleus; *Pcm*, peduncle of the mamillary body; *Pp*, crusta; *Pu*, putamen; *Pul*, pulvinar; *Stri*, intermediate layer; *TII*, optic tract; *Tpt*, transverse tract of the peduncle; *Tri*, inter-cranial trigone; *VIII*, third ventricle; *VS*, bundle of Vieq d'Azyr. Weigert's stain. $\times 1\frac{1}{2}$. (After Marburg.)

"*centre median*," or nucleus of Luys, a small oval cell group lying just dorso-lateral from the red nucleus, and separated from it by a narrow interval of white matter; the lateral cell mass or lateral nucleus; a ventral group of cells; a small anterior nucleus; a dorsal cell group; a large rounded posterior extremity, the pulvinar; together with several nuclei of minor importance.* The

* The limited space at our disposal, and the indeterminate state of our present knowledge of the relations of these several cell groups to the fibre paths of the brain, does not warrant a detailed description of the subdivisions of the optic thalamus. For its minute structure, so far as it is at present known, the reader is referred to the excellent text-books of Barker and Obersteiner, and to the works of Nissl, von Monakow, and Marburg.

optic thalami of the two hemispheres are united with each other by the *posterior commissure*, which bridges across the third ventricle.

The *caudate nucleus* lies dorso-lateralward from the optic thalamus, which latter body it partially encircles. It projects into the wall of the lateral ventricle, and is separated from the optic thalamus by a thin band of white matter.

The optic thalamus and caudate nucleus, on the mesial side, are separated from the more laterally situated lenticular nucleus by a broad band of white matter, the cerebral continuation of the pyramids, fillet, and other long fibre tracts of the mesencephalon.



FIG. 392.—A SECTION OF THE HUMAN BRAIN STEM AT THE MID-LEVEL OF THE OPTIC THALAMUS.

Ce, external capsule; *Cex*, capsula extrema; *Ci*, internal capsule; *Cl*, claustrum; *Coa*, anterior commissure; *Coao*, olfactory bundle to the anterior commissure; *Fo*, fornix; *fol*, olfactory bundle of Zuckerkandl; *glp*, globus pallidus; *Gorb*, orbital convolutions of the cortex; *I*, island of Reil; *Lmm*, lateral medullary layer of the thalamus; *Nc*, caudate nucleus; *Ndm*, dorsal nucleus of the thalamus; *Nl*, lateral nucleus of same; *Nm*, mesial nucleus of same; *Pu*, putamen; *rcc*, fronto-occipital bundle; *Ssc*, stratum subcallosum; *St*, stria cornea; *Tt*, tænia thalami; *Va*, bundle of Vieq d'Azyr; *VIII*, third ventricle. Weigert's stain. $\times 1\frac{1}{2}$. (After Marburg.)

The important bundle thus inserted between the basal nuclei is known as the *internal capsule*.

As seen in horizontal section the internal capsule, conforming to the convex surface of the thalamus, makes a sharp bend. Based upon this fact, the tract is arbitrarily divided into a knee, a posterior limb, and an anterior limb. In transverse, viz., frontal, section this bend is not seen, the white fibres are continued directly into the medullary white substance of the cerebral hemisphere in a radiating manner, thus forming the *corona radiata*.

The *lenticular nucleus* forms the ventro-lateral boundary of the internal capsule. It is connected with its fellow of the opposite side by a compact bundle, the *anterior commissure*. This nucleus is divisible into a lateral portion, the *putamen*, and a mesial portion, the *globus pallidus*.

Lateral from the lenticular nucleus, and separated from it by the thin external capsule of white matter, is a flattened mass of grey matter, the *claustrum*. This nucleus lies just mesial to the *island of Reil* (*gyrus seu lobus insulæ*).

At a somewhat lower level, in the angle between the ventral surface of the pyramids as they pass lateralward into the internal capsule, and the mesial border of the lenticular nucleus, lies the optic tract on its way to the posterior border of the thalamus, where it enters the *lateral geniculate body*. This small ovoid body lies just ventro-lateral to the pulvinar, the *medial geniculate body* occupying the angle between the pulvinar and the corpora quadrigemina.

In the interior of the brain-stem, in an area bounded ventrally by the pyramids and dorsally by the red nuclei and optic thalami, is the diencephalic continuation of the long fibre paths of the mesencephalic tegmentum. In front of this area is the cephalic end of the substantia nigra Sömeringi, and more lateralward the *hypothalamic nucleus*. This nucleus in transection presents an oval mass of small nerve cells. The *zona incerta*, the cephalic continuation of the formatio reticularis, is interposed between the red nucleus, on its dorsal side, and the substantia nigra and hypothalamic nucleus, which form its ventral boundary.

From the lateral surface of the nucleus ruber, a heavy bundle of fibres, the probable continuation of the path of the superior cerebellar peduncles by means of secondary neurones whose cells lie in the red nucleus, is directed lateralward toward the ventro-

lateral nuclei of the thalamus. This fibre bundle is ill-defined and soon blends with the mesial lemniscus or fillet, whose fibres, turning upward to reach the middle of the posterior limb of the internal capsule, lie in relation with the ventral surface of the optic thalamus.



FIG. 393.—A FRONTAL SECTION THROUGH THE INTERNAL CAPSULE AND CORONA RADIATA OF MAN.

C, fissure of Rolando; *CA*, Ammon's horn; *Ca*, ascending frontal convolution; *Cell*, corpus callosum; *Ce*, external capsule; *Cex*, capsula extrema; *Ci*, internal capsule; *Clm*, callosal-marginal fissure; *Cng*, cingulum; *Coa*, anterior commissure; *Cp*, ascending parietal convolution; *Cr*, corona radiata; *Csth*, hypothalamic nucleus of Luys; *Fa*, fascia dentata; *fFp*, fronto-pontine tract; *Fm*, fimbria; *Fls*, inferior longitudinal fasciculus; *Fo*, fornix; *For*, arcuate fasciculus; *Frn*, gyrus fornicatus; *frtf*, Meynert's fasciculus; *Fs*, superior frontal convolution; *fs*, superior frontal sulcus; *gfp*, globus pallidus; *H*, Forel's field; *Hl*, hippocampal gyrus; *I*, island of Reil; *III*, oculomotor nerve; *Narc*, arcuate nucleus; *Nc*, caudate nucleus; *Nl*, lateral nucleus of the thalamus; *Nm*, median nucleus of same; *Ngr*, red nucleus; *Oti*, inferior occipito-temporal sulcus; *Otl*, inferior occipito-temporal convolution; *Po*, pons; *Pu*, putamen; *ree*, fronto-occipital bundle; *Rop*, optic radiation; *S*, fissure of Sylvius; *SnS*, substantia nigra; *ssc*, stratum subcallosum; *ssc*, tapetum; *St*, stria cornea; *Ts*, inferior temporal convolution; *ti*, inferior temporal sulcus; *TII*, optic tract; *TL*, median longitudinal striæ; *Tm*, middle temporal convolution; *tm*, middle temporal sulcus; *Ts*, superior temporal convolution; *ts*, superior temporal sulcus; *Tt*, tænia thalami; *Tte*, tænia tecta; *U*, uncus; *VL*, lateral ventricle; *Vlh*, inferior horn of same. Weigert's stain. × 14. (After Marburg.)

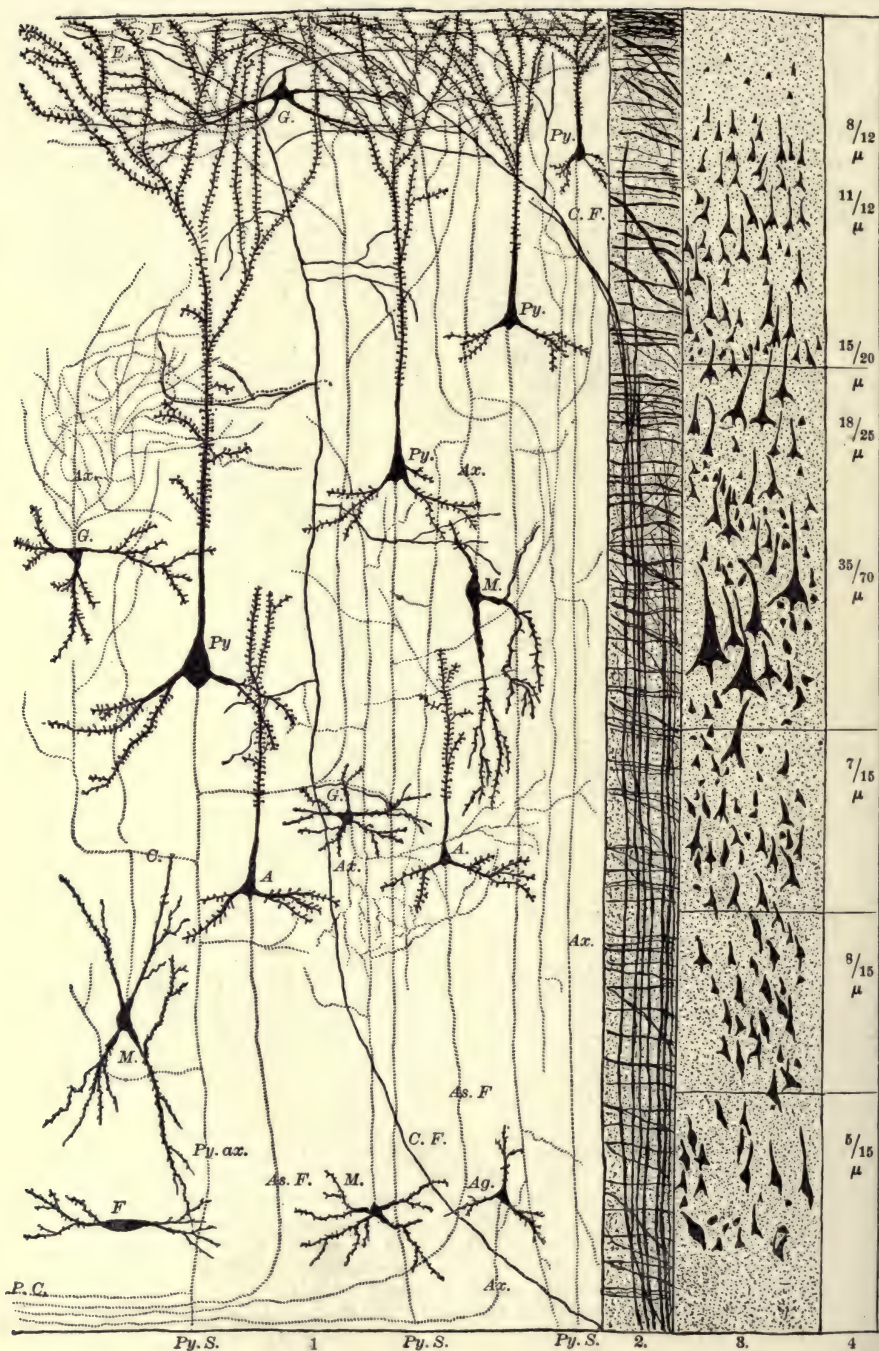


FIG. 394.

THE CEREBRUM.—Frontal sections through the entire breadth of the cerebrum, at the region of the thalami, show the continuation of the corona radiata into the white medulla of the cerebral hemispheres, the entire radiation being surrounded by the grey matter of the cerebral convolutions (*cerebral cortex, pallium*) as by a mantle.

The white matter of the cerebral medulla, besides the many fibres of the corona radiata, contains an innumerable number of short fibres which bring the nerve cells of all portions of the grey cortex into intimate conduction relation with each other. These fibres collectively form the cerebral association paths; the nerve cells from which their fibres are derived likewise form the *association centers* of the cerebrum as distinguished from the *projection centers*, whose nerve fibres enter the corona radiata.

Many of the association fibres, in their passage from center to center, form definite bundles, which may be arbitrarily classified into three groups. 1. Some bundles connect corresponding portions of opposite cerebral hemispheres, e. g., corpus callosum, anterior commissure, hippocampal commissure (fornix commissure, or psalterium). 2. Some connect different lobes of the same hemisphere, e. g., inferior longitudinal fasciculus, fronto-occipital fasciculus, fronto-parietal fasciculus, and the superior longitudinal fasciculus or fasciculus arcuatus. 3. Numerous arcuate fibres pass beneath the sulci to connect the nerve cells of adjacent convolutions.

The nerve cells which enter into the formation of the grey matter of the cerebral cortex present a remarkable tendency to arrange themselves in more or less well-defined layers parallel to the surface of the cerebral convolutions. The number and arrangement of these layers in the various lobes varies, however, with the peculiar function of each of these areas. Thus, in the motor area there is a five layer type, in the parietal lobe a seven layer type, in the occipital lobe a six or eight layer type.

FIG. 394.—SCHEME OF THE MOTOR AREA OF THE CEREBRAL CORTEX, SHOWING THE EFFECT OF VARIOUS STAINING METHODS.

1, Golgi's stain; 2, Weigert's stain; 3, hematein and eosin; 4, relative depth of each layer. *A*, association cells; *Ag*, angular cells of the polymorphous layer; *As F*, association fibres; *Ax*, neuraxes; *C*, collateral; *C F*, centripetal fibres; *E*, terminal fibres; *F*, fusiform cell of the polymorphous layer; *G*, Golgi cells, Type II; *M*, cells of Martinotti; *PC*, collateral of a pyramidal cell; *Py*, pyramidal cells; *Py ax*, neuraxis of a pyramidal cell; *Py S* pyramidal neuraxes passing to the cerebral medulla. (After Berkley.)

In general, it may be assumed that the nerve cells of all of these layers are included in one or two physiologically distinct groups or types those whose neuraxes enter the projection paths, and those whose neuraxes enter the association paths; also that while these cells intermingle with each other in all portions of the cortex, yet certain areas are characterized by an undue proportion of one or the other type, and may accordingly be considered as either projection centers or association centers.

The larger cells belong, as a rule, to the projection centers, and the peculiar type of large cell contained in a given center may often be considered as characteristic of that particular area. Thus the motor area contains giant pyramidal cells, the visual area has the giant "solitary cells" of Meynert, and the cornu Ammonis contains large bipolar spindle cells.

The larger cells, being of Golgi's Type I, are assumed to be connected with the projection fibres. On the other hand, the smaller cells—granule cells, polymorphous cells, etc.—which more frequently belong to Golgi's Type II, are thought to supply the neuraxes of association paths. Those large areas—parietal lobe, frontal lobe, lobulus insulæ—which consist in so large a part of the smaller type of cells, may therefore be supposed to contain the larger association centers.

The cells in any given portion of the cortex are not only arranged in layers parallel to the surface of the cerebral convolutions, but the passage of fibres of the corona radiata and white medulla to or from their terminations within the pallium, also separates the cells of the cortex into irregular rows or striations, whose axis is perpendicular to the surface of the convolutions.

IN THE MOTOR AREA the cortical cells form five tangential layers, as follows:

1. Molecular layer.
2. Outer polymorphous cell layer.
3. Small pyramidal cell layer.
4. Large pyramidal cell layer.
5. Inner polymorphous cell layer.

The molecular layer consists of a network of fine dendritic fibres, derived from the deeper layers, which are disposed in tangential meshes beneath the pia mater. Occasionally small cells, apparently displaced from the deeper cell layers, are scattered among these fibres; they are of polymorphous form, and their processes are confined to the molecular layer. The surface of the molecular

layer is covered by a *marginal veil* of neuroglia homologous with that beneath the pia mater of the spinal cord.

The second, or outer polymorphous cell layer, is a thin stratum. Its cells are frequently clumped, thus forming groups of various size. This grouping is, however, more distinct in some other regions, e. g., the olfactory area, than in the motor area itself.

The third layer, small pyramidal cells, is somewhat thicker than the above. It consists of numerous small cells—triangular, pyramidal, or pyriform in shape—whose pointed apices are directed toward the surface. Three sets of dendrites are given off by these cells, an apical process which passes outward to ramify in the outer molecular layer, and from either side of the base of the cell a second set, whose processes are distributed in a plane nearly corresponding to that in which their cell bodies lie. The neuraxis is usually given off from the basal surface of the cell, and passes from this point directly inward to the white matter of the cerebral medulla. These small pyramidal cells are not very deeply stainable, and according to the classification of Nissl fall under the parapyknomorphic arkyochrome variety.

The fourth layer, that of the large pyramidal cells, is also a thick layer. Its cells are of the same shape, and distribute their processes after the same manner as those of the small pyramidal cell layer. According to the classification of Nissl, however, these giant pyramids are deeply stainable, or pyknomorphic arkyochrome cells. The motor area is specially characterized by the large size of the cells of this layer.

The fifth, or inner polymorphous cell layer, is thinner than the preceding. Its cells are of very varied form—pyramidal, stellate, fusiform, and granule cells—and are less densely packed than is

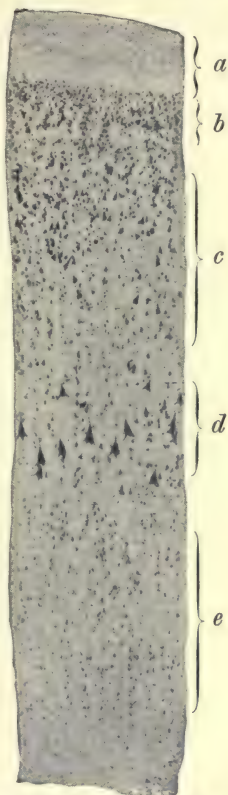


FIG. 395.—HUMAN CORTX
CEREBRI, MOTOR AREA.

a, tangential fibre layer;
b, outer polymorphous cells;
c, small pyramidal cells; *d*,
large pyramidal cells; *e*,
inner polymorphous cells.
Nissl's stain. Moderately
magnified. (After Schlapp.)

the case in the more superficial layers. They are intermediate in size, between the cells of the second and the third layers. The neuraxes of the inner polymorphous cells, in large part, pass to the white matter of the medulla, though some of them are distributed laterally to neighboring convolutions. Their dendrites are partially distributed within the layer in which they arise, but by far the larger portion pass to the more superficial pyramidal

cell layers. Many of the nerve cells of this layer, e. g., the granule cells, are without a distinct rim of cytoplasm, and are therefore cytochrome, according to Nissl. The larger forms—stellate, pyramidal, and fusiform—are parapyknomorphic arkyochrome cells.

It is noticeable that, as a rule, the dendritic processes from the cells of all five layers are distributed either in the same plane as their cell bodies, or they pass toward the surface, where many of them enter the superficial molecular layer. The neuraxes, on the other hand, are directed inward toward the white matter of the cerebral medulla, in which they pass, either as association or as projection fibres, to many very distant parts. Notable exceptions to this latter rule, however, are the so-called cells of Martinotti, which occur to some extent in all layers, but which, though found in the pyramidal layers, are especially numerous among the polymorphous and granule cells. They are small polymorphous cells, which send their neuraxes to the superficial molecular layer, giving off collaterals on their way.

The cell types in other portions of the cortex correspond very closely to those of the motor area. There are, however, slight but characteristic variations which are worthy of notice.



FIG. 396.—HUMAN CORTEX CEREBRIS, PARIETAL LOBE.

a, tangential fibre layer; *b*, outer polymorphous cells; *c*, small pyramidal cells; *d*, outer large pyramidal cells; *e*, granule cells; *f*, inner large pyramidal cells; *g*, inner polymorphous cells; *h*, white matter of the medulla. Nissl's stain. Moderately magnified. (After Schlapp.)

THE CORTEX OF THE PARIETAL LOBE (also of the *frontal*, *temporal*, convex surface of the *occipital* lobes, and the *insula*)

presents a seven layer type, the additional layers resulting from an aggregation of the granule cells into one plane, which thus divides the large pyramidal cell layer. This type, therefore, presents the following layers:

1. Molecular or tangential fibre layer.
2. Outer polymorphous cell layer.
3. Small pyramidal cell layer.
4. Outer large pyramidal cell layer.
5. Granule cell layer.
6. Inner large pyramidal cell layer.
7. Inner polymorphous cell layer.

The distribution of this cortical type is suggestive of a close relation to the great association centers. Moreover, its most noticeable characteristics are the abundance of its granule cells and the relative paucity of pyramidal cells, especially those of the giant pyknomorphic variety.

IN THE VISUAL AREA—median surface of the occipital lobe—the formation is described as either a six or an eight layer type. The pyramidal cell layers are reduced to extreme thinness, the giant pyramids being noticeably deficient. The stripes of Baillarger, thin layers of tangential fibres on the deeper portions of the cortex, are especially distinct. So many granule cells are scattered among those of the pyramidal type that it becomes scarcely possible to distinguish from one another the second, third, and fourth layers. When these three layers are individually considered, the type presents eight layers; if, on the other hand, they are collectively considered as a single stratum, the type presents but six layers.

With this reservation, the following layers may be distinguished:



FIG. 397.—HUMAN CORTEX CEREBRI, OLFACTORY REGION.

a, tangential fibre layer; *b*, white matter of the medulla. Nissl's stain. Moderately magnified. (After Schlapp.)

larger, the thick fibre layer in the deeper part of the molecular stratum, the abundance of granule cells, the paucity and irregular form of the pyramidal cells, and finally the presence in the inner stripe of Baillarger and in the outer portion of the deep polymorphous cell layer of numerous large isolated multipolar cells, the giant "*solitary cells*" of *Meynert*.

IN THE AUDITORY AREA—temporal lobe—the seven layer type is found. Its structure in this area is apparently identical with that previously described for the seven layer type in the parietal lobe.

IN THE RHINENCEPHALON several peculiarities of cell formation are found. That occurring in the olfactory bulbs will be briefly considered in connection with the course of the olfac-

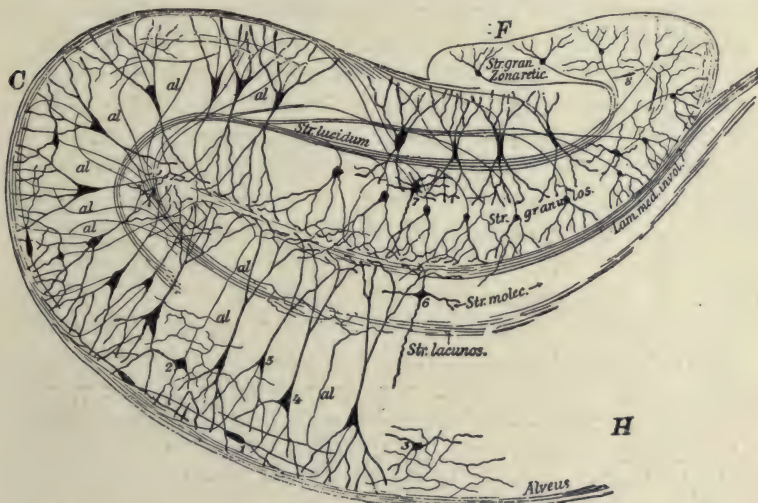


FIG. 399.—DIAGRAM OF THE CORNU AMMONIS AS SHOWN BY THE GOLGI STAIN.

al, collaterals of the pyramidal cells; *C*, Ammon's horn; *F*, dentate fascia; *H*, hippocampal gyrus. 1-8, typical cells of the several layers; 1, fusiform; 2, 3, small polymorphous; 4, 5, pyramidal; 6, small polymorphous; and 7, 8, cells of the dentate fascia. (After K. Schaffer, from Piersol.)

tory tracts (page 555). The olfactory area of the hippocampal gyrus and the peculiar formation of the cornu Ammonis deserve mention at this time.

IN THE HIPPOCAMPAL GYRUS the outer polymorphous cells exhibit a special tendency to group formation. The pyramidal cells form a tier of considerable thickness, but are of irregular shape. The cortex as a whole is comparatively thin. It presents the following layers:

1. The molecular fibre layer.
2. The grouped polymorphous cell layer.
3. The layer of irregular pyramidal cells.
4. The inner polymorphous cell layer.

Ammon's horn presents a peculiar formation, which may be considered as forming a transition area between the cerebral cortex and the very thin fascia dentata. The cornu Ammonis is characterized by the special prominence of but one cell type, the pyramidal, this cell layer forming the greater part of its thickness.

Its basal layer, the *alveus*—homologue of the cerebral medulla—is continuous with the white matter of the gyrus hippocampus. Within the alveus is a thin molecular layer, the *stratum oviens*, homologous with the polymorphous cell layer; it contains a very few small fusiform cells. The basal processes of the pyramidal cells penetrate this layer to spread out within the alveus.

Next to the stratum oviens is the broad *pyramidal cell layer*, its cells lying in the basal portion of the layer and sending their processes toward the alveus. From the apices of these cells a second set of processes pass toward the outer molecular layer, their thicker stem portions producing the radial appearance from which this part has been called the *stratum radiatum*.

The small pyramidal and outer polymorphous cell layers are merely represented by an unusually vascular, molecular layer containing a very few small nerve cells. The abundance of small anastomosing blood vessels in this layer gives it a lacunar appearance, hence its name—the *stratum lacunosum*.

The true *molecular layer* is the next beyond the lacunar stratum, and is similar in structure to its homologue in other parts of the cerebral cortex. On the surface of this layer, replacing the pia mater, is the *lamina medullaris involuta*, which contains the terminal dendrites of the pyramidal cells; it is therefore homologous with the superficial tangential fibres of the molecular layer in other portions of the cerebral cortex.

To recapitulate, the layers of Ammon's horn are as follows:

- | | |
|--------------------------------|--------------------------|
| 1. Lamina medullaris involuta. | 5. Pyramidal cell layer. |
| 2. Molecular layer. | 6. Stratum oviens. |
| 3. Stratum lacunosum. | 7. Alveus. |
| 4. Stratum radiatum. | |

THE CEREBELLUM.—The cortex of the cerebellum, like other portions of grey matter, consists of nerve cells with their naked processes, together with their supporting neuroglia. The grey

matter is distributed over the surface of the convolutions, and incloses the medullary white matter. The latter consists of medullated nerve fibres passing to or from the cortical cells.

In section the cortex presents two distinct layers separated by a border line of large pyriform nerve cells, the *cells of Purkinje*. The outer layer, *molecular stratum*, contains many cell

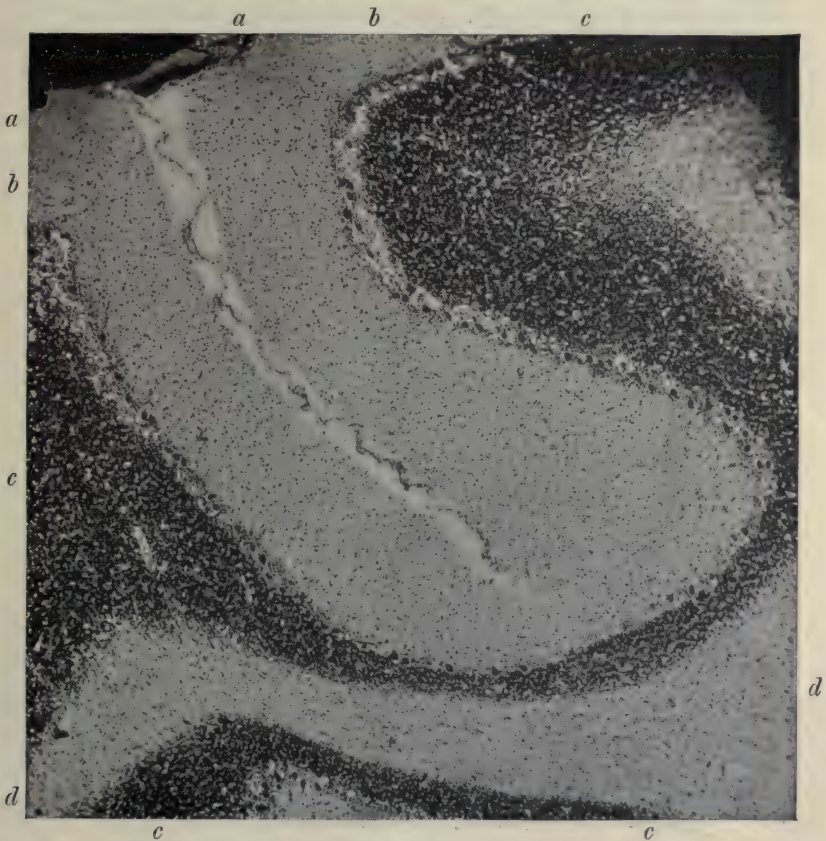


FIG. 400.—FROM A SECTION OF THE CEREBELLAR CORTEX OF MAN.

a-a, pia mater; *b-b*, molecular layer; *c-c*, granular layer; *d-d*, white matter of the medulla. Nissl's stain. Photo. $\times 38$.

processes but few cell bodies. The inner, *granular* or *nuclear layer*, on the other hand, consists almost entirely of small nerve cells with prominent nuclei, together with glia cells.

The Nuclear Layer.—The nerve cells of the granular or nuclear layer contain large spherical nuclei which are surrounded by the

narrowest possible rim of cytoplasm. From the cytoplasm of each cell a few short and slender dendrites and a very fine neuraxis are given off. The dendrites interlace among the neighboring cells of the granular layer. The neuraxes pass outward to the molecular layer, in the middle and outer portion of which they divide, in a T-like manner, to form two terminal branches which are distributed in the long axis of the cerebellar convolution.

Many glia cells also occur in the granular stratum, their radiating fibres extending through the entire depth of the layer. This stratum is penetrated by the neuraxes of the Purkinje cells on their way to the medulla, and by nerve fibres coming from the medulla which lose their medullary sheath on entering the granu-

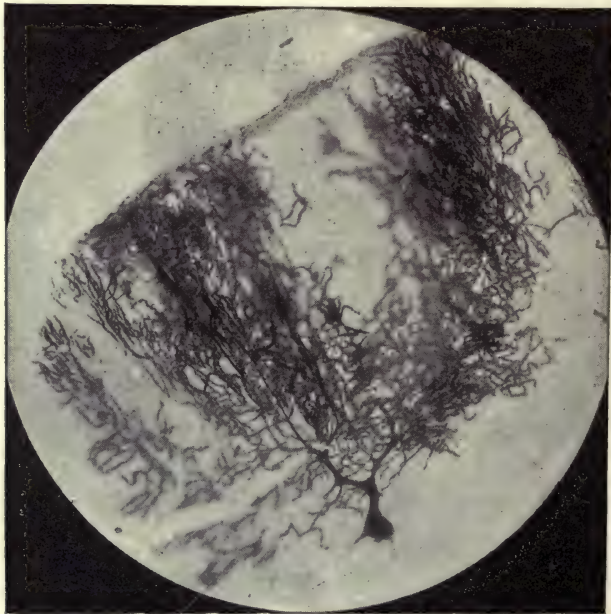


FIG. 401.—A PURKINJE CELL FROM THE HUMAN CEREBELLAR CORTEX.
Moderately magnified. Photo. (After Berkley.)

lar layer, and terminate by end brushes in relation either to the granule cells or to the cells of Purkinje.

The granular layer is thickest at the apex of the convolution, and thinnest opposite the bottom of the sulci. This peculiarity apparently results from the infolding of the cortex in the course of that portion of its development during which the sulci are formed.

Those portions of the cortex which are thus carried in with the sulci are necessarily attenuated.

The cells of Purkinje form the characteristic element of the cerebellar cortex. These are very large pyriform nerve cells, placed between the nuclear and the molecular layers, with their long axis nearly perpendicular to the adjacent surface of the convolutions. From their inner pole a neuraxis arises, and, penetrating the nuclear layer, enters the white medulla, where it acquires a medullary sheath. In its passage through the nuclear layer the neuraxis gives off recurrent collaterals which return into the molecular layer to terminate in relation to neighboring cells of Purkinje.

A thick-stemmed dendrite arises from the outer pole of the Purkinje cell, but immediately divides into two primary branches. Occasionally the two branches are given off directly from the cell body. From these primary branches smaller processes pass into the molecular layer and dicotymously divide into an innumerable number of fine terminal fibrils. This arborization is peculiar in the absence of anastomoses, and in the fact that it lies entirely within the limits of a plane whose diameter is no greater than that of the cell body, a plane which is found in the transverse axis of the cerebellar convolution. It is therefore impossible to demonstrate this arborization in sections which are cut parallel to the long axis of the convolution. The bodies of the Purkinje cells are closely surrounded by a basketwork of terminal fibrils derived from the cells of the molecular layer.

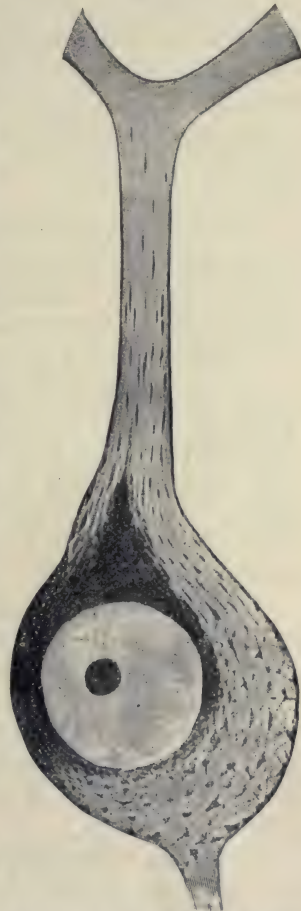


FIG. 402.—A PURKINJE CELL FROM THE CEREBELLAR CORTEX OF THE RABBIT.

Highly magnified. (After Nissl.)

The molecular layer consists chiefly of the processes of cells which are found in the deeper layers; it possesses but few cells of its own. Such nerve cells as it may possess, though all of small size, fall under two types, the one whose processes spread out lateralward and interlace with the dendrites of Purkinje's cells, and the other whose processes pass transversely through the cerebellar convolutions and give off collaterals which dip inward to form end baskets around the bodies of the Purkinje cells. The neuraxes of these latter cells, in the tangential portion of their course, form a stratum of fibres which occupies the deeper third of the molecular layer and overlies the outer poles of the Purkinje cells.

Glia cells also occur in the molecular layer, many of them distributing their processes in planes perpendicular to the surface of the convolutions. These glia fibres penetrate the entire depth of the molecular layer, and on the surface of the convolutions beneath the pia mater form a superficial "*basal membrane*."

The greater part of the molecular layer is composed of fibres which, however, are not only derived from the intrinsic cells of this layer, but also include processes from Purkinje's cells and from the granule cells of the nuclear layer, together with certain fibres which enter from the white matter of the medulla and terminate in a network about the chief dendrites of Purkinje's cells.

According to the classification of Nissl, nearly all the nerve cells of the cerebellar cortex, with the exception of Purkinje's cells, are of the cytochrome variety; their nucleus stains deeply, and corresponds in size to that of a leucocyte; mere traces of cytoplasm are present. Nevertheless, a few cells of the granular layer possess a much larger nucleus, one which equals in size that of the average nerve cell; they are therefore of the karyochrome type of Nissl.

Purkinje's cells come under the arkyo-stichochrome or arkyochrome variety (Nissl*), their large granules of stainable substance being arranged in the form of an indistinct network whose meshes are more or less parallel to the nuclear membrane and to the surface of the cell. These coarse granules are continued outward into the dendrites; they also frequently form a "nuclear cap" for that pole of the nucleus which adjoins the stem of the dendrite.

* Allg. Zeitschr. f. Psychiät., 1898.

It is a remarkable fact that the only cells of the cerebellar cortex which send their neuraxes into the white medulla are those of Purkinje. All the other nerve cells appear to be so arranged as to serve as association paths only, whereas the neuraxes of the Purkinje cells may be said to form the projection paths of the cerebellar cortex.

CHAPTER XXV

THE NERVOUS SYSTEM (*Continued*)

C. THE CONDUCTION PATHS OF THE CENTRAL NERVOUS SYSTEM

THE functions of the central nervous system, as well as the interpretation of its lesions, all center around its capacity for the transmission of nerve impulses, the process of conduction. Hence the importance of tracing with certainty the histological paths by which these impulses are conveyed.

These paths are divisible into three general classes:

1. Centrifugal or "motor" tracts.
2. Centripetal or "sensory" tracts.
3. Association tracts.

The centrifugal tracts are so arranged as to conduct nerve impulses in a direction from the cerebral cortex toward the peripheral nerve endings; the centripetal conduct from the periphery toward the cerebral cortex; while the association paths connect not only the opposite sides of the central organs by commissural fibres, but pass between different levels of the spinal cord and brain and may even unite very remote parts—e. g., the nuclei of the midbrain and the ventral horns of the spinal cord.

A. The Motor Paths

The centrifugal or motor paths begin in the motor area of the cerebral cortex and include the neuraxes of all those pyramidal nerve cells which occur in the grey matter of this area. These neuraxes penetrate the deeper layers of the cortex and as projection fibres enter the corona radiata of the cerebral medulla. Here, they converge toward the knee of the internal capsule, which they enter in a compact bundle. They then pass beneath the optic thalamus to enter the crusta of the midbrain as the large pyramidal bundles.

In the midbrain and pons the pyramidal tracts coming from the two cerebral hemispheres converge toward the median line. In

the pons, however, they are broken up by the transverse pontal fibres into numerous small bundles of large medullated fibres. At the lower border of the pons these bundles reunite to form a compact bundle, on either side of the median line, which enters the pyramids of the medulla oblongata.

Thus far the course of the motor tracts has been entirely ventral. In the lower part of the medulla a marked change in this condition is produced as a result of the motor decussation. About ninety per cent of the motor fibres which have been traced into the pyramids of the medulla now change their direction, pass obliquely inward, dorsalward, and spinalward, decussate in the median line with their fellow of the opposite side, and enter the lateral columns of the spinal cord, where they form the crossed pyramidal tracts.

Not more than ten per cent of the fibres of the pyramidal tracts in the medulla,* on the other hand, continue straight into the ventral columns of the spinal cord as the direct or uncrossed pyramidal tract. This uncrossed fasciculus takes a position on either side of the anterior median fissure. However, the fibres of this tract constantly decussate through the ventral or white commissure of the spinal cord in the cervical region, so that the tract becomes progressively smaller and smaller in its passage down the cervical cord, and below this region is seldom found. Its fibres end in arborizations about the ventral horns of the opposite side. Thus all the fibres of the motor paths to the spinal cord reach the opposite side as compared with the cerebral hemisphere in which they arise. The fibres of the crossed as well as those of the direct pyramidal tracts end in arborizations about the ventral horn cells of the spinal cord.

The neuraxes of the motor cells of the ventral horns in each

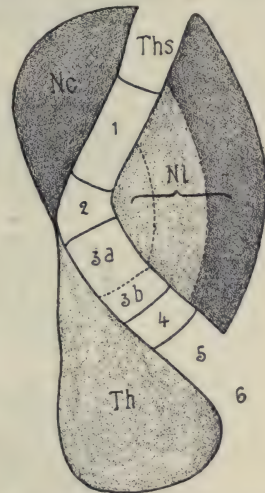


FIG. 403.—DIAGRAM OF THE INTERNAL CAPSULE.

Nc, caudate nucleus; *NL*, lenticular nucleus; *Th*, optic thalamus; *Ths*, anterior stalk of the thalamus; 1, fronto-pontal path; 2, cortico-bulbar path; 3a, cortico-cervical path; 3b, cortico-lumbar path; 4, path of muscular sense; 5, temporo-pontal path; 6, optic radiation. (After Obersteiner.)

* Usually less than ten per cent; the volume of decussation within the medulla oblongata is subject to very great individual variation.

spinal segment pass ventralward in small bundles and make their exit from the antero-lateral sulcus. Outside the cord they unite to form the ventral roots of the spinal nerves.

In a similar manner the motor roots of the cranial nerves, with the exception of the abducens, are connected with the motor paths.

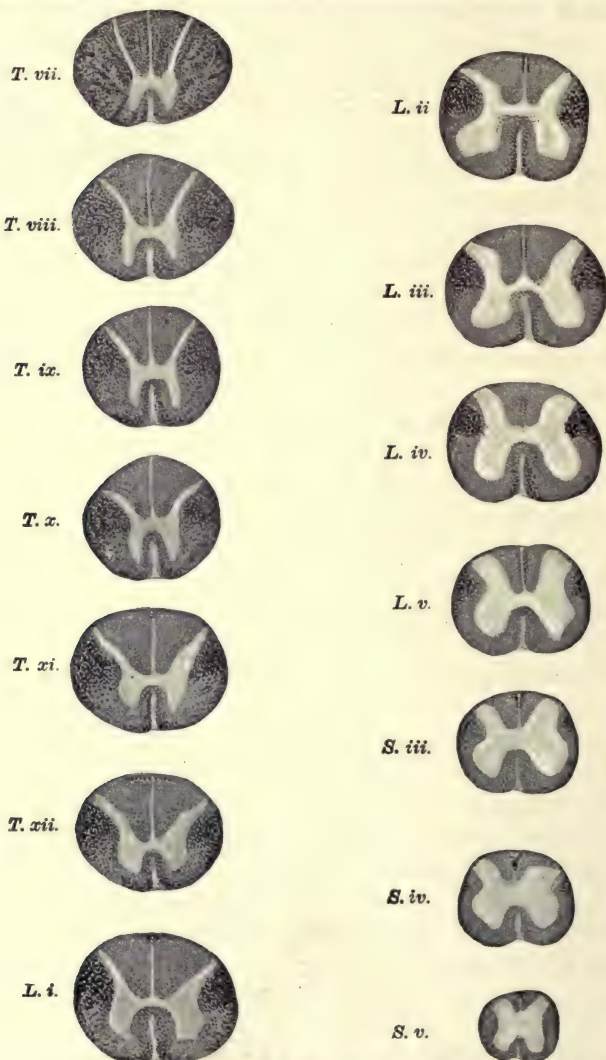


FIG. 404.—THE MOTOR PATHS OF THE SPINAL CORD AS SHOWN IN A CASE OF DESCENDING DEGENERATION BELOW A TRANSVERSE LESION AT THE LEVEL OF THE SEVENTH THORACIC SEGMENT. Marchi's stain. (After Hoche.)

Primary neurone fibres leave the motor tract at a level a little above that of the cranial nerve root, pass dorsalward along the median raphé, decussate, and pass directly to the motor nucleus of the cranial nerve about whose cells they form terminal arborizations.

The motor path is thus seen to consist of two distinct sets of neurones, a central and a peripheral. The cell body of the central or primary motor neurone lies in the motor area of the cerebral cortex; the terminal arborizations of its fibres and collaterals surround the nerve cells of the motor nuclei of the cranial and spinal nerves. A second neurone, the peripheral or secondary motor neurone, arises from these cells, enters the motor nerve root as a medullated nerve fibre, and passes by means of the cranial or spinal nerve trunk to its peripheral nerve ending in muscle, epithelium, etc.

It is a noteworthy fact that there is one and only one decussation in any given fibre tract of the motor path; this decussation, for the spinal nerves, occurs in the central neurone either at the great motor decussation of the medulla oblongata or through the ventral commissure of the cervical region of the spinal cord. There is no decussation in the peripheral neurone of the motor path. Since every central motor neurone almost without exception decussates somewhere in its course, the peripheral nerve ending of each fibre tract of the motor path lies on the opposite side of the body from its origin in the motor area of the cerebrum.

The motor tracts may be traced in the adult by means of histological sections taken after destruction by operation, injury, or disease of the motor area in the cerebrum, which thus causes degeneration of the entire central neurone, or by a similar destruction of the motor nuclei of the cranial nerves or ventral horns of the spinal cord, which produces degeneration of the peripheral neurones arising from these motor nuclei.

In the fetus the central motor neurones acquire their myelin sheaths at a very late period (in great part after birth), and are thus readily distinguished from the centripetal paths, which become medullated at a much earlier stage.

B. The Sensory Paths

The centripetal or "sensory" paths are more complicated than the motor in that their central neurones—which are multiple instead of single—follow one of four different central paths, whereas the central motor neurones, as we have seen, follow a common

path from the cerebral cortex to the cell body of the peripheral neurone.

The peripheral or primary sensory neurones all follow a homologous path. Their cell body lies in the dorsal root ganglion of a

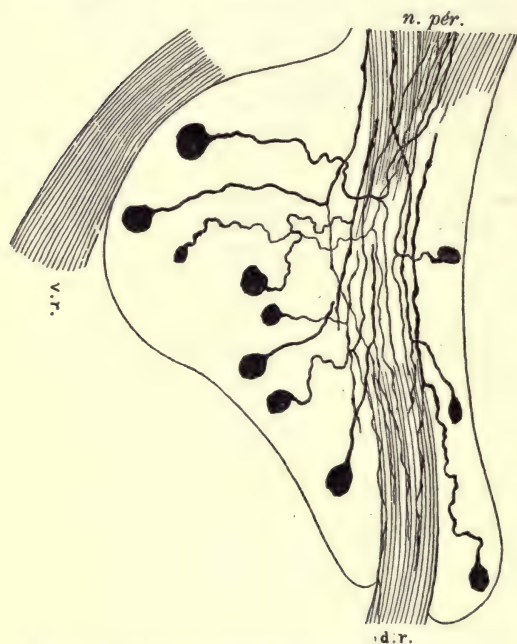


FIG. 405.—A GANGLION OF A DORSAL NERVE ROOT OF A MOUSE, AS SHOWN BY THE METHOD OF GOLGI.

d. r., dorsal root; *n. pér.*, peripheral spinal nerve; *v. r.*, ventral root. (After van Gehuchten.)

spinal nerve or in the cerebro-spinal ganglion of a cranial nerve (e.g., jugular, petrosal, and cochlear ganglia). The nerve cells of these ganglia possess a single process which immediately divides in a Y- or T-like manner into a peripheral and a central branch.

The peripheral process enters the distal part of the posterior spinal nerve root and follows the course of the cerebro-spinal nerve to its termination at the peripheral end organ. The central process enters the proximal part of the nerve root and thus reaches the spinal cord

or brain. Once within the central nervous system it divides by a Y or T branch into a short and a long process, the longer being always directed toward the medulla oblongata. Hence in the spinal nerves the long process passes cephalad, the short caudad. The reverse occurs in the cranial nerves, the long process is caudad in direction and the short is cephalad.

Both long and short processes end according to the same plan, yet their difference in length results in the appearance of long ascending and short descending peripheral neurone tracts in the spinal cord while in the brain the corresponding descending tracts are the longer.

The peripheral neurones of the cranial nerves end by arboriza-

tion about the cells of their sensory nuclei. A second neurone, sensory neurone of the second order, enters the tract of the fillet and

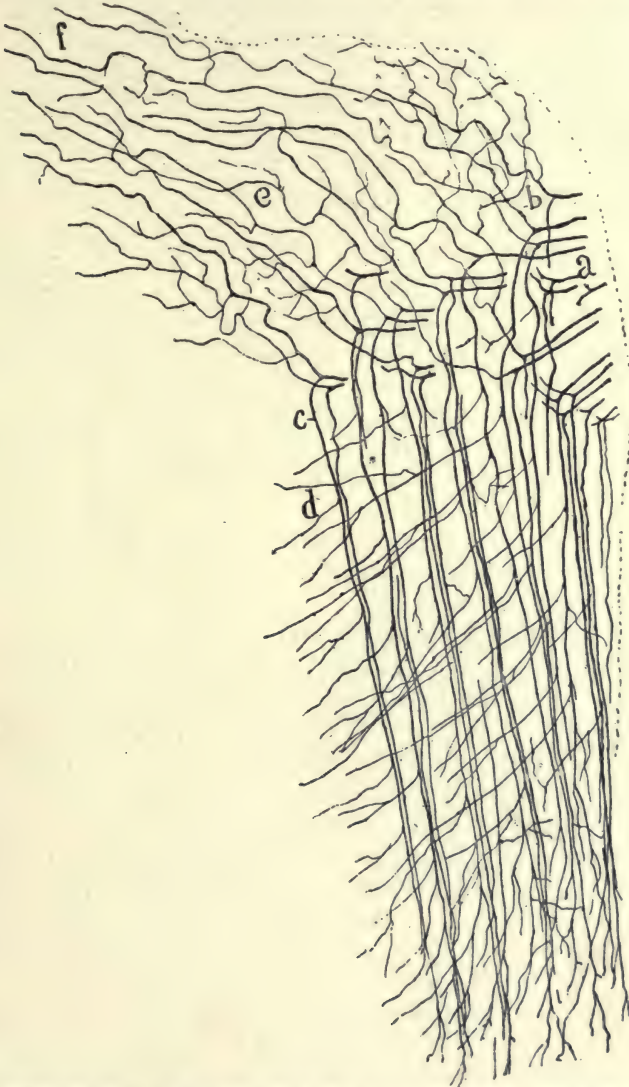


FIG. 406.—SAGITTAL SECTION THROUGH THE LATERAL PORTION OF THE PONS VAROLII OF A FETAL MOUSE, SHOWING THE BIFURCATION OF THE CENTRAL PROCESSES OF THE PERIPHERAL SENSORY NEURONES OF THE VESTIBULAR NERVE.

a, central processes; *b*, *e*, *f*, ascending branches; *c*, descending branches; *d*, collaterals. Golgi's stain. (After Ramón y Cajal.)

passes cephalad to be continued to the cerebrum by means of neurones of the third or even higher orders.

In the spinal cord the peripheral sensory neurones—sensory neurones of the first order—enter as dorsal root fibres and divide into their long ascending and short descending branches.* This division is thought to occur in the dorso-lateral column, where many of the short descending branches unite to form the so-called *comma tract*. This tract consists of a group of nerve fibres, the most of which, after injury, degenerate downward for a short distance.

The descending branch, after a short course, enters the grey matter of the dorsal horns, and afterward follows a course exactly similar to such of the ascending branches as also reach the grey matter of the spinal cord. The further course of these fibres may be considered as conforming to one of four paths.

I. They may pass obliquely cephalad through the postero-external column (Burdach's tract) to enter the postero-median column or tract of Goll, in which they travel upward to the medulla oblongata.

II. They may enter the grey matter and pass directly to the ventral horns, with end arborizations in relation to the cells of this region (reflex tracts).

III. They may enter the grey matter and end directly with terminal arborizations about the cells of Clarke's vesicular cell column.

IV. They may enter the grey matter and promptly end in relation to the nerve cells of the dorsal horns and intermediate zone.

PATH "I"—Burdach's tract, nearly identical with the anatomical postero-external column, contains incoming fibres of the posterior spinal nerve roots and is divisible into several root zones which were first mapped out by Flechsig † from embryonic tissues.

A ventral root zone, semilunar in shape, adjoins the grey commissure and the ventral third of the dorsal horns. It contains endogenous fibres which probably connect the posterior horn cells of opposite sides (cornu-commissural tract). This is the last of the root zones to become medullated in the embryo.

* It is a peculiar and also an important fact that the fibres of the dorsal roots as they pierce the pia mater to enter the spinal cord, lose temporarily their medullary sheaths, thus forming a constricted band at this point, and leaving the almost naked neuraxes without protection from the vicissitudes of vascular pressure. Once through the pia mater their medullary sheath is promptly restored.

† Leipzig, 1876.

A medio-lateral root zone adjoins the posterior two-thirds of the dorsal horns and contains the compact bundles of the posterior nerve roots on their way to the grey matter.

The comma tract of Schultze occupies the mesial side of the middle third of Burdach's column and adjoins the lateral aspect of the postero-internal column or tract of Goll. It is thought to contain the short descending branches of incoming posterior nerve root fibres, and perhaps also intrinsic or endogenous fibres which pass up or down to connect neighboring segments of the spinal cord. The medio-lateral zone together with the comma tract forms the greater part of the middle root zone.

The dorsal root zone contains, on its outer side, the fine ascending and descending fibres derived from the dorsal nerve roots which form the tract of Lissauer. This bundle occupies a small area in the lateral portion of the dorsal root zone.

The mesial portion of the dorsal root zone includes a large area in which are those posterior root fibres which pass obliquely upward through the tract of Burdach to a higher level, where they enter the tract of Goll (postero-internal column). As a result of their oblique direction, those root fibres which enter the lower segments of the spinal cord will, upon reaching the tract of Goll, lie nearest the median line; those which enter higher spinal segments necessarily arrive later in the tract of Goll and are thus forced to take a more lateral position in their further course to the medulla oblongata.

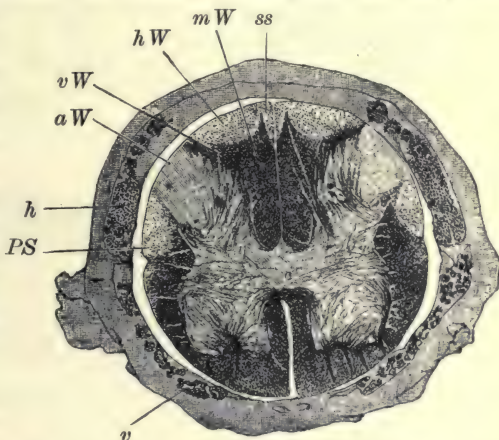


FIG. 407.—UPPER HALF OF LUMBAR ENLARGEMENT OF A FETUS 35 CM. LONG.

a W, dorsal root zone (lateral portion) of dorsal funiculi (Lissauer's fasciculus); *h*, dorsal roots, partly medullated; *h W*, dorsal root zone (medial portion); *m W*, middle root zone; *PS*, lateral pyramidal tract; *ss*, dorsal root zone (most median part of medial portion) of dorsal funiculi; *v*, ventral roots, medullated; *v W*, ventral root zone of dorsal funiculi. (After Flechsig.)

The group of dorsal root fibres which thus follows the tract of Goll to the medulla oblongata ends by terminal arborizations about

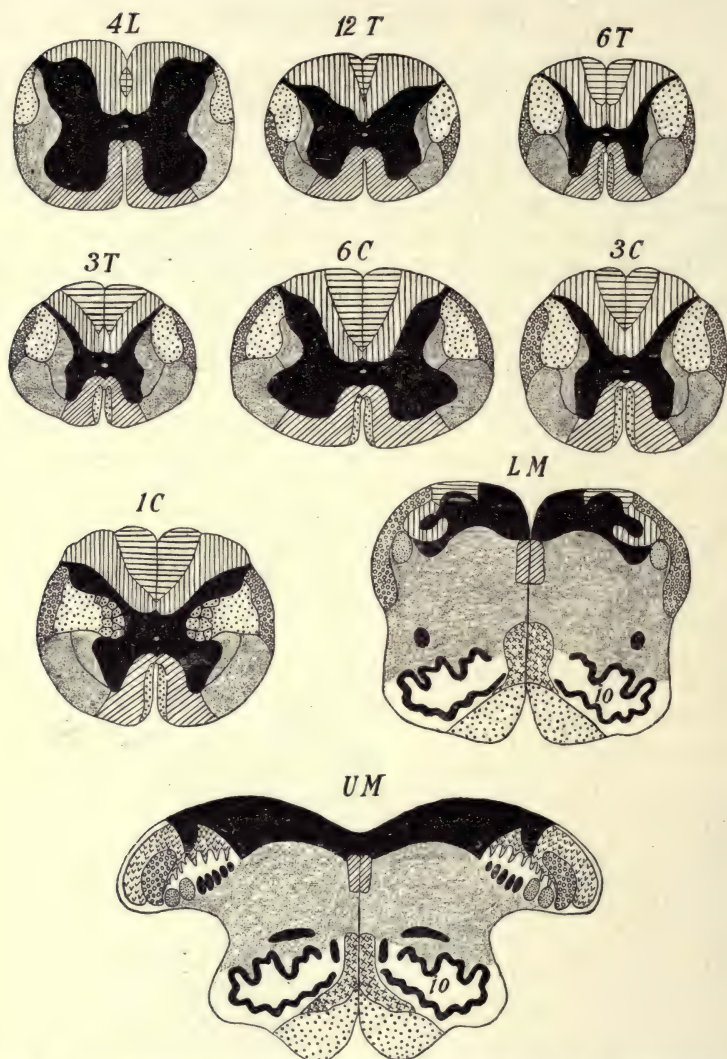


FIG. 408.—DIAGRAMMATIC REPRESENTATION OF THE TRACTS OF THE SPINAL CORD AND THEIR RELATION TO THE PATHS OF THE MEDULLA OBLONGATA.

• *C*, cervical, *L*, lumbar, and *T*, thoracic segments of the spinal cord; the prefixed number indicates more exactly the level; *LM*, lower, and *UM*, upper segments of the medulla; *io*, inferior olivary body; in the lower medulla the lateral nuclei are shown just behind the olive; in the upper medulla the accessory olivary nuclei are shown.

	Column of Goll.		Lateral ground bundles, and tract of Gowers.
	Column of Burdach.		Direct cerebellar tract.
	Anterior ground bundle, continuous in the medulla with the posterior longitudinal bundle.		Spinal root of the auditory nerve, and the cerebello-olivary fibres.
	Pyramidal (motor) tracts.		Mesial fillet, interolivary portion.
	Spinal root of the trigeminus (seen only in <i>LM</i> and <i>UM</i>).		Grey matter.

the cells of the nucleus of Goll. They convey the nerve impulses of muscular sensation and are chiefly derived from those nerves which come from the limbs. The column of Goll, therefore, first attains an appreciable size in the lumbar region, but adds to its volume in each successive spinal segment through which it passes. In the cervical region, this influx of fibres is so great that the entire volume can scarcely be contained within the limits of the postero-internal column, and many are forced to continue their course in the column of Burdach until they reach the medulla oblongata where they end by arborization about the nerve cells of the nucleus of Burdach.

From the nuclei of Goll and Burdach, neurones of the second order send their neuraxes ventralward toward the opposite side, the larger portion taking a direct course as internal arcuate fibres through the *formatio reticularis alba* to the raphé, where they decussate to the opposite side and immediately turn upward between the inferior olivary bodies to form the first portion of the mesial fillet or lemniscus. This early portion of the lemniscus, because of its position, is known as the *interolivary fillet*.

The smaller portion of the neurones of the second order from the nuclei of Goll and Burdach follow the indirect course, as external arcuate fibres, first passing dorsalward to reach the surface of the medulla oblongata, which they then follow ventralward, keeping close beneath the pia mater until they reach the margin of the pyramidal tracts, where they divide, a small portion passing between the pyramids and the olivary body, a larger portion passing around the ventral and mesial borders of the pyramids to reach the median raphé. Here the two bundles reunite, join the internal arcuate fibres, decussate to the opposite side, and enter the interolivary portion of the mesial fillet.

The mesial fillet in this portion forms a flattened band on either side of the median line, its dorsal margin blending with the posterior longitudinal fasciculus, a similar though smaller bundle of association fibres which will be described under a later heading. The longitudinal fibres of the fillet are spread over a sectional area which extends from the mid-region of the inferior olives dorsalward nearly to the hypoglossal nucleus, the posterior longitudinal fasciculus being interposed between this nucleus and the dorsal margin of the fillet.

The mesial fillet begins at the level of the nucleus of Goll and increases rapidly in size in its upward course by the constant addi-

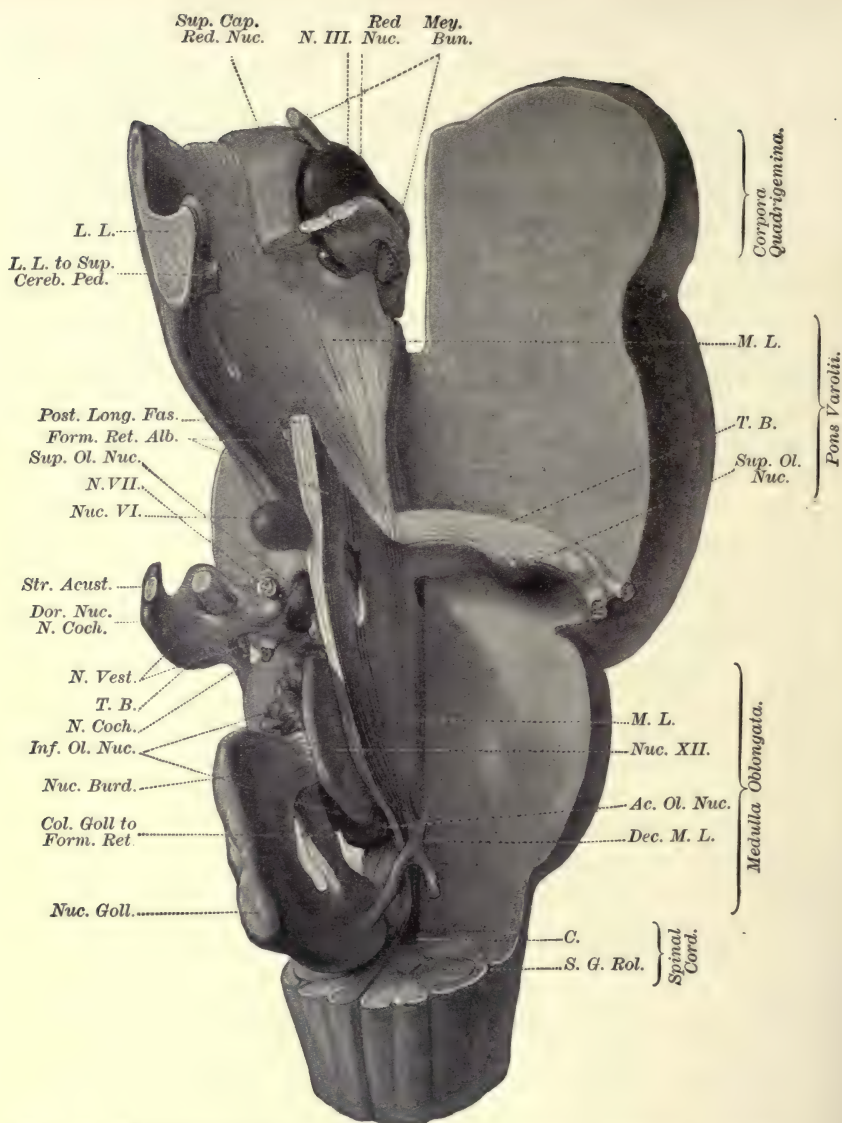


FIG. 409.—RECONSTRUCTION OF THE MEDULLA OBLONGATA AND MIDBRAIN OF A CHILD.

Ac. Ol. Nuc., accessory olivary nucleus; *C.*, central canal of the spinal cord; *Col. Goll to Form. Ret.*, bundle passing from the column of Goll to the formatio reticularis alba; *Dec. M. L.*, decussation of the mesial lemniscus through the internal arcuate fibres; *Dor. Nuc.*, dorsal nucleus of the cochlear nerve; *Form. Ret. Alb.*, formatio reticularis alba; *Inf. Ol. Nuc.*, inferior olivary body; *L. L.*, lateral lemniscus; *L. L. to Sup. Cereb. Ped.*, bundle passing from the lateral lemniscus to the superior cerebellar peduncle; *M. L.*, interolivary portion of the mesial lemniscus; *Mey. Bun.*, fasciculus retroflexus of Meynert; *N. III.*, root of the oculomotor nerve; *N. VII.*, root of the facial nerve; *N. Coch.*, root of the cochlear nerve; *N. Vest.*, root of the vestibular nerve; *Nuc. VI.*, nucleus of the abducens nerve; *Nuc. XII.*, hypoglossal nucleus; *Nuc. Burd.*, Burdach's nucleus; *Nuc. Goll.*, nucleus of Goll; *Post. Long. Fas.*, posterior longitudinal bundle; *Red Nuc.*, red nucleus; *S. G. Rol.*, gelatinous substance of Rolando; *Str. Acust.*, striæ acusticæ; *Sup. Cap. Red. Nuc.*, superior capsule of the red nucleus; *Sup. Ol. Nuc.*, superior olivary body; *T. B.*, trapezoid body. (After Sabin.)

tion of the arcuate fibres already described, and, later, of similar fibres from the cranial nerves. It forms the chief sensory or centripetal pathway, and, as it continues the impulses received from "Path I" of the spinal cord, it contains neurones of the second order, whose cell bodies lie in the nuclei of Goll and Burdach. Neurones of the second and higher orders coming from the sensory nuclei of the cranial nerves join the fillet in the medulla oblongata and mid-brain.

In the pons Varolii the mesial fillet also forms a flattened ribbon on either side of the median raphé, but gradually assumes a more ventral position, thus becoming separated from the posterior longitudinal fasciculus which makes a dorsal curve in its passage through the medulla and pons.

In the upper portion of the pons the mesial fillet lies in the ventral part of the tegmentum, but spreads somewhat lateralward, becoming thus twisted upon itself, so that the long diameter of its sectional area now lies in the transverse axis of the pons instead of being in the ventro-dorsal axis as in the medulla oblongata.

In the mesencephalon the tracts of the mesial fillet become still more divergent. They now occupy the lateral margin of the tegmentum where their dorso-lateral margin blends with the newly formed *lateral fillets*.*

In the diencephalon the paths of the fillet continue their divergent course. They pass to the optic thalami where many of their fibres have end arborizations. Many of the fillet fibres also have "relay stations," as it were, all along their course—e. g., in the formatio reticularis of the medulla oblongata and pons Varolii, and in the grey matter of the hypothalamic region—from which they are continued by neurones of higher orders to, or possibly beyond, the thalami.

From the optic thalami, by neurones of the third or higher orders, the path of the fillet is continued into the posterior limb of the internal capsule just behind the motor tract; thence they follow the radiations of the corona radiata to the cerebral cortex.

The tract of the fillet acquires many fibres throughout its extensive course, which, though all centripetal and therefore subject to ascending degeneration, are of very diverse function and consequently possess a very broad distribution within the cerebral cortex.

* The lateral fillet is a portion of the central auditory path which enters the medulla through the cochlear portion of the eighth cranial nerve.

PATH "II."—The second subdivision of the dorsal nerve roots includes many fibres and collaterals from the dorsal root

fibres which enter the grey matter from the medio-lateral root zone and pass directly to the ventral horns, where they end in relation with the dendrites or cell bodies of the large motor cells. This group of fibres forms the great pathway for reflex impulses. It includes descending branches of the peripheral sensory neurones as well as collaterals from many of their ascending branches.

PATH "III."—Beginning in the lumbar region and extending upward through the greater portion of the thoracic spinal cord is a sharply defined oval cell column, situated in the grey matter at the base of the dorsal horn where it joins the grey commissure on either side of the median line; this group is the "*vesicular cell column of Lockhart Clarke.*"

In the lower lumbar and sacral regions a similarly situated but smaller and less well defined group of nerve cells is found in the base of the dorsal horns, and forms the so-called "*nucleus of Still-*

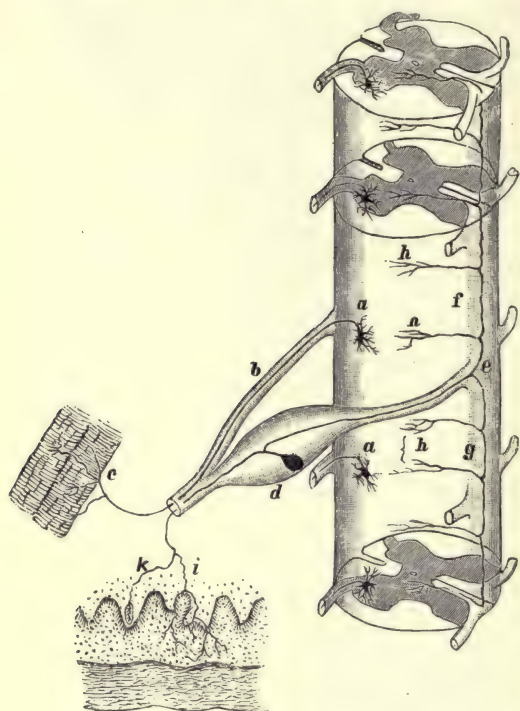


FIG. 410.—DIAGRAM OF THE ORIGIN AND RELATIONS OF THE PERIPHERAL MOTOR AND SENSORY NEURONES.

A cylindrical section of the spinal cord, with its ventral and dorsal nerve roots, is shown. *a*, nerve cell of the ventral horn whose neuraxis passes through the ventral nerve root, *b*, to its peripheral termination, *c*; at *d*, is a unipolar sensory nerve cell in the dorsal root ganglion; its process immediately divides into a peripheral and a central branch. The central branch enters the spinal cord and at *e*, divides into an ascending, *f*, and a descending, *g*, branch from both of which numerous collaterals, *h*, enter the grey matter and terminate in fine end brushes. The peripheral branch of the spinal ganglion cell enters a spinal nerve and finds its way to its termination which is here represented in the skin; it terminates partly by free endings among the epithelial cells, *i*, and partly in connection with a sensory end organ, *k*, in this case a tactile corpuscle of Meissner. (After von Lenhossék.)

ing."* Its cells possess similar connections and are similar in function to those of Clarke's column.

About the cells of these nuclei the third division of the dorsal root fibres have their terminal arborizations. The central neurone of this path, sensory neurone of the second order, begins with the cells of Clarke's column, and to a much less extent from those of Stilling's nucleus; their neuraxes pass obliquely outward and upward to reach a point near the surface of the lateral white columns. Here they form a thin ribbon-like superficial zone which spreads forward from the dorsal nerve roots to a point opposite the central grey commissure. This superficial fibre bundle is the *dorso-lateral* or *direct cerebellar tract*, so called because of its location in the spinal cord and because of the distribution of its fibres, which pass directly cephalad to the medulla oblongata, and thence through the superficial zone of the restiform body of the same side to the vermis of the cerebellum. It is therefore, as are all other paths from the spinal cord to the cerebellum, an uncrossed or direct tract.

Those fibres of the direct cerebellar tract which enter at the lower levels naturally assume the more superficial position. Moreover, since Clarke's column is not found as a distinct nucleus above the thoracic region, the direct cerebellar tract does not appreciably increase in size above this level. The neurones of this path probably transmit impulses which are chiefly derived from the abdominal and thoracic viscera, hence it receives few fibres in the cervical portion of the spinal cord.

In the vermis cerebelli the terminal arborizations of fibres coming from the direct cerebellar tract are undoubtedly in relation, either directly or by collaterals, with the cerebellar cortex. However, the majority at least of its impulses leave the cerebellum through the superior cerebellar peduncles by means of neurones of the third order, decussate in the mesencephalon, and in great part terminate in the red nucleus of the opposite side.

It is thought, however, that some of the neurones of the superior cerebellar peduncles extend beyond the red nucleus without interruption. These uninterrupted fibres are joined by the nerve fibres of those sensory neurones of the fourth order, whose cell bodies lie in the red nucleus, and together they continue the path through "Forel's field," enter the posterior limb of the internal capsule in relation with the fillet tract, and travel thence through the corona radiata to the cortex cerebri.

* Cassel, 1859.

PATH "IV."—The fourth and last division of the dorsal root fibres follows a somewhat more uncertain course. The neuraxes of its peripheral neurones end in arborizations about the many small cells in the dorsal horns of the spinal cord, on the same, and possibly also to some extent on the opposite side. Thence they pass up the spinal cord by neurones of higher orders, which form association bundles in the lateral columns and thus connect the dorsal horn cells of successively higher levels. In the brain these paths have been traced into the *formatio reticularis*.

A considerable number of dorsal horn cells in the spinal cord send their neuraxes into a narrow superficial zone in the anterior half of the lateral column to form the *ventro-lateral ascending column* or *tract of Gowers*. This tract, increasing in size, continues up the spinal cord to the lateral column of the medulla oblongata. Its further course is somewhat uncertain, though it undoubtedly continues upward through the lateral portion of the *formatio reticularis* in the pons, where some of its fibres turn sharply backward and enter the vermis cerebelli through the middle, and possibly also the superior, cerebellar peduncles; other fibres continue upward through the *formatio reticularis* to the optic thalamus (Hoche*). From this point its impulses probably reach the cortex of the cerebral hemisphere after the same manner and in company with the fibres of the preceding division (**PATH "III"**).

C. The Association Paths

Besides the motor and sensory paths of the central nervous system there are certain other tracts which connect the nuclei of various levels. Some of these are tracts of ascending, some of descending degeneration. Many of them, however, contain both ascending and descending fibres and may be called mixed fibre tracts.

Some of the above tracts contain long fibres, e. g., the sulco-marginal fasciculus, while others, e. g., the antero-lateral ground bundles of the spinal cord, consist chiefly of short fibres. The course of many of these association fibres is so difficult to follow that they are not yet well known. We shall only attempt, therefore, to trace briefly the course of the more important fasciculi, first those of the spinal cord and later those of the brain.

The comma tract of Schultze in the middle root zone of the posterior white column has already been mentioned as probably con-

* Arch. f. Psychiat., 1896.

taining association fibres which connect the posterior horn cells of adjacent levels. This tract is most prominent in the cervical region. It is absent from the lower portions of the spinal cord.

The posterior white column in the sacral region of the spinal cord contains a small bundle which, with its fellow of the opposite side, forms an oval or cuneate area which incloses the posterior median septum. This short tract is the **fasciculus dorso-medialis** (*dorso-medial sacral bundle, triangle médian, Flechsig's oval field*). Though part of its fibres are thought to come from the dorsal roots and are therefore exogenous, yet many are undoubtedly derived from the more cephalad regions of the spinal cord. This fasciculus is therefore homologous with those fibres which at higher levels are found in the comma tract.

In the lateral white column are four distinct tracts, the intermedio-lateral fasciculus, the lateral border zone, the lateral ground bundle, and Helwig's fasciculus.

The intermedio-lateral fasciculus (*rubro-spinal tract, von Monakow's bundle*) occupies a small area at the ventral margin of the crossed pyramidal tract. The fibres of this bundle probably arise in the optic thalamus and red nucleus of the opposite side. They decussate in the tegmentum and reach the spinal cord through the formatio reticularis of the pons and medulla. The fasciculus extends the entire length of the spinal cord, its collaterals being distributed to the ventral horns.

The lateral border zone is a thin area adjoining the lateral surface of the grey matter of the spinal cord. Its short fibres connect the nerve cells of neighboring spinal segments.

The lateral ground bundle includes many fibres, some ascending and some descending, which connect more distant segments of the spinal cord, and in the medulla oblongata blend with the anterior ground bundle to enter the formatio reticularis alba and posterior longitudinal fasciculus.

Helwig's fasciculus is a short tract, found only in the cervical region. It is triangular, or at times crescentic in section, and lies in front of the broad apices of the ventral horns at the ventral margin of the lateral white columns. The origin and destination of these fibres is not yet known.

The anterior white column contains the sulco-marginal fasciculi and an anterior or ventral ground bundle.

The descending sulco-marginal fasciculus (*Löwenthal's tract*) in the cervical region occupies an area just ventral to the direct py-

ramidal tract. As the size of this latter path diminishes with its passage caudalward, the sulco-marginal fasciculus moves backward along the anterior median sulcus into the position thus vacated. In the thoracic and lumbar regions the tract under discussion occupies the narrow area on either side of the anterior median fissure which in the cervical region contains the direct pyramidal tract.

The fibres of the fasciculus take origin in the anterior corpus quadrigeminum of the opposite side, decussate through Meynert's commissure, pass caudad in a position which is ventral to the aqueduct of Sylvius and the posterior longitudinal fasciculus, and enter the anterior column of the spinal cord. The bundle in passing receives many neuraxes from the cells of Deiters' nucleus in the rhombencephalon. The fibres derived from Deiters' nucleus, therefore, form a large portion of those which form this tract. The fasciculus sulco-marginalis extends the entire length of the spinal cord, its collaterals being probably distributed to the ventral horns.

The ventral portion of this fasciculus also contains many ascending fibres which are thought to arise in the nerve cells of the dorsal horns and intermediate zone of the opposite side. They then decussate through the anterior commissure and pass cephalad either as scattered fibres among those of the descending sulco-marginal fasciculus or as a small bundle in the ventral margin of this tract. These fibres form the *ascending sulco-marginal fasciculus*.

The anterior ground bundle forms a large portion of the anterior white columns. Like the lateral ground bundle, it connects neighboring segments of the spinal cord and is similarly continued into the medulla oblongata. In fact, the course of these two bundles is so entirely comparable that they may be, and frequently are, collectively described as the *antero-lateral ground bundle*.

The formatio reticularis alba of the medulla oblongata receives, among its many fibre bundles, certain fibres from the antero-lateral ground bundles of the spinal cord which continue cephalad through the reticular formation of the pons and midbrain for a varying distance. In the medulla and midbrain they are probably connected with a small cell group which in each of these locations lies in or near the median line: these are the *superior and inferior central nuclei*. The ultimate destination of this group of fibres is, however, still obscure.

The Posterior Longitudinal Fasciculus.—Certain other fibres from the antero-lateral ground bundles of the spinal cord, as they enter the formatio reticularis of the medulla oblongata, unite to

form a compact fibre bundle, the posterior or median longitudinal fasciculus. This fasciculus presents a gentle dorsal curve in its passage through the medulla oblongata, in the upper part of which

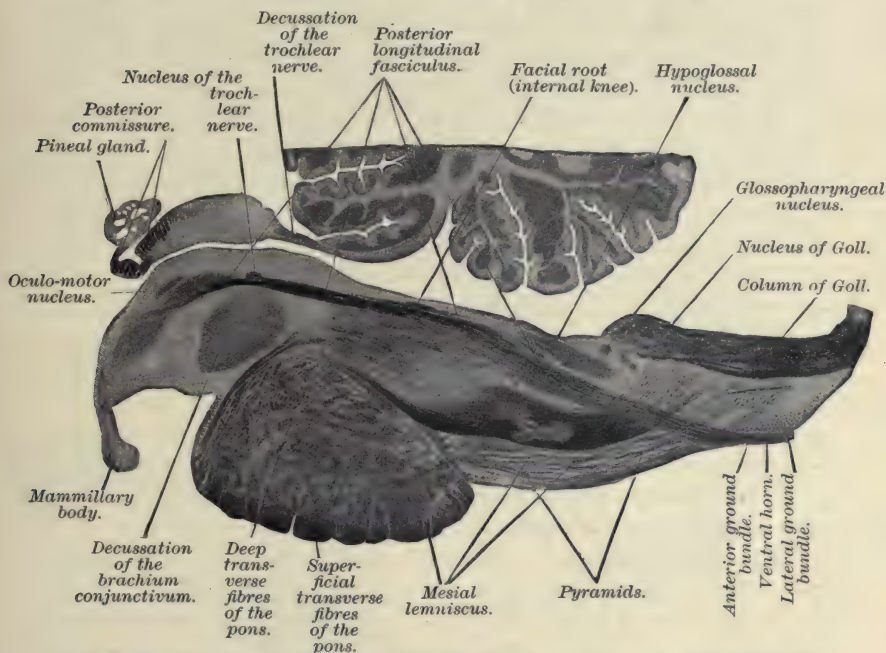


FIG. 411.—A SAGITTAL SECTION OF THE MEDULLA OBLONGATA, PONS, AND MESENCEPHALON PARALLEL AND CLOSE TO THE MIDDLE LINE, FROM A CHILD AGED THREE MONTHS.

The posterior longitudinal fasciculus and its relation to the antero-lateral ground bundle of the spinal cord are particularly well shown. Weigert's stain. (After Bruce.)

it reaches a position near the median raphé, and just in front of the dorsal grey matter of the hypoglossal nucleus. Here it blends with the dorsal margin of the interolivary portion of the mesial fillet.

As it enters the pons Varolii the posterior longitudinal bundle separates from the fillet, thus attaining a still more dorsal position, in which it continues its course through the pons. In the midbrain it lies ventral to the aqueduct of Sylvius, but makes a gradual ventral curve which corresponds to the increased depth of the grey matter surrounding the aqueduct at this level. The fasciculi of either side, together form a median trough in which the nuclei of the oculo-motor nerve are found.

In the diencephalon the posterior longitudinal fasciculus apparently ends in the *nucleus of Darkschewitsch* or *nucleus of the posterior longitudinal fasciculus*.

Though we have traced the course of this fasciculus from the spinal cord cephalward, it must be borne in mind that it contains fibres which run both cephalad and caudad, and that it is therefore subject to both ascending and descending degeneration.

In its course through the brain the posterior longitudinal fasciculus receives many fibres from the sensory nuclei of the cranial nerves, especially from those of the ocular group with which it is in close relation. By these connections the several groups of ocular nuclei are brought into intimate relation with one another as well as with those nuclei of closely related function which occur in the cervical region of the spinal cord.

The *cerebellum* possesses at least three important association paths, the one placing this organ in relation with the opposite inferior olivary body through the cerebello-olivary tract, the second connecting it with the opposite cerebral hemisphere through the superior cerebellar peduncles, and the third placing the cerebellum in communication with the medulla oblongata and midbrain through the middle cerebellar peduncles.

The cerebello-olivary tract arises from nerve cells in the vermis cerebelli, and, passing caudad through the restiform body, enters the medulla oblongata. Its fibres here turn sharply inward and ventralward in small discrete bundles and penetrate the formatio reticularis, lying more lateral but parallel to the internal arcuate fibres. Most of the bundles decussate to the opposite side and enter the inferior olivary body, many of them first traversing the surface of this nucleus. The fibres which thus surround the inferior olive form for it an encapsulating sheath of medullated nerve fibres. A few fibres of the cerebello-olivary tract end without decussation in the inferior olivary body of the same side.

The superior cerebellar peduncle (*brachium conjunctivum*) takes origin from the cells of the vermis cerebelli and enters the mesencephalon as a large round bundle of fibres which, at first, forms the lateral roof of the fourth ventricle, but gradually sinks ventralward, thus passing obliquely around the lateral border of the grey matter which surrounds the aqueduct of Sylvius. The bundle finally makes a sharp mesial curve toward its decussation at the cephalic end of the mesencephalon. Its position is thus mesial and dorsal to that of the mesencephalic portion of the fillet.

After decussation the fibres of the brachium conjunctivum are immediately lost in the red nucleus of the opposite side. A few of its fibres, however, are said to continue past the red nucleus without interruption. These, together with neuraxes from the cells of the nucleus ruber, enter Forel's field, and pass lateralward either to the optic thalamus or to the lenticular nucleus. Their further course is uncertain, but it seems probable that from these points new neurones continue the path through the corona radiata to the cerebral cortex. Each cerebellar hemisphere is thus placed in intimate relation with the opposite half of the cerebrum.

The path of the brachium conjunctivum, like all the other association tracts, contains fibres which run in both directions. It is therefore a tract of more or less mixed degeneration.

The Middle Cerebellar Peduncles.—Fibres from the cerebellum also enter the middle cerebellar peduncles and pass to the crusta of

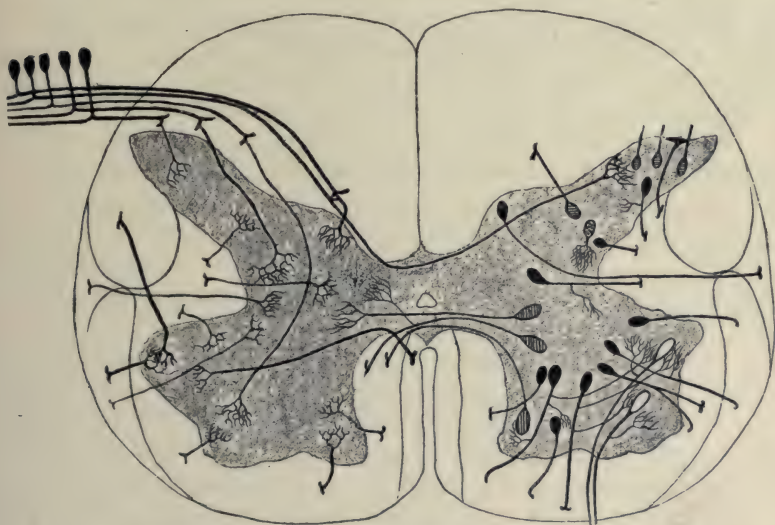


FIG. 412.—DIAGRAM OF THE FIBRE PATHS OF THE SPINAL CORD.

The black cells are of the sensory or centripetal paths, those on the left are spinal ganglion cells whose branches may be traced to their several terminations within the spinal cord. The motor cells of anterior horn on the right are white; commissural cells are vertically striped; the small cells of the dorsal horns are horizontally striped; a small "Golgi cell" of the dorsal horn is stippled. (Redrawn after the scheme of von Lenhossék.)

the pons, where they end in terminal arborizations about those nerve cells, of the same and opposite sides, which are scattered

through this portion of the pons Varolii. Through these *pontal nuclei* the cerebellum is brought into relation with the association paths of the mes- and rhombencephalon.

The more important conduction paths of the spinal cord may at this time be summarized as follows :

	DESCENDING	ASCENDING
In the posterior column.	Comma tract.† Dorso-lateral sacral bundle.†	Goll's tract.† Burdach's tract.†
In the lateral column.	Crossed pyramidal tracts.* Intermedio-lateral fasciculus.‡	Dorso-lateral cerebellar tract.† Ventro-lateral cerebellar tract.†
In the anterior column.	Direct pyramidal tract.* Descending sulco-marginal fasciculus.‡ Helwig's fasciculus.‡	Ascending sulco-marginal fasciculus.‡

* In the motor pathway.

† In the sensory pathway.

‡ Association paths.

CHAPTER XXVI

THE NERVOUS SYSTEM (*Continued*)

D. THE CENTRAL PATHS OF THE CRANIAL NERVES

THE course of the *spinal nerves* has already been sufficiently described in tracing the course of the great motor and sensory paths of the spinal cord. Each spinal segment was found to contain the nuclei of a ventral or motor nerve root, whose centrifugal peripheral neurones begin in its ventral horns, together with certain cell groups of the posterior horns and intermediate zone which serve as sensory nuclei, receive the end arborizations of peripheral sensory neurones whose nerve cells lie in the spinal ganglion of a dorsal nerve root, and send their neuraxes cephalad in one of the various centripetal tracts of the spinal cord. In the medulla these centripetal paths unite in the fillet, by which, with the aid of neurones of higher orders, the centripetal impulses are finally conveyed to the cerebral cortex.

The course of the *cranial nerves*, while conforming quite closely to the same general arrangement, presents slight deviations from this type which result in the appearance of special nuclear groups and centripetal pathways. These peculiarities warrant a brief outline of the central paths of the several cranial nerves.

The twelfth or hypoglossal nerve (Figs. 383 and 384) contains only centrifugal or "motor" fibres. This nerve takes its origin in the large-celled *hypoglossal nucleus*, which is ovoid in shape, and is situated in the medulla oblongata on either side of the median line and just dorsal to the posterior longitudinal fasciculus (Fig. 383). The nucleus can be traced through the lower half of the medulla, and if it is stained according to the method of Weigert, it can be readily distinguished by the many coarse medullated fibres which it contains.

The central neurones of the hypoglossal nerve come down from the cerebrum in the pyramidal tracts. Having arrived at the level

of the nucleus they turn sharply dorsalward along the median raphé, pass between the interolivary fillets, and thus reach the region of the hypoglossal nucleus, where they turn sharply outward, to end by arborization around its cells.

The peripheral neurones of the twelfth cranial nerve begin with the large cells of the hypoglossal nucleus. Their neuraxes pass directly ventralward in large bundles and make their exit from an antero-lateral groove between the pyramid and the inferior olivary body.

The eleventh or spinal accessory nerve (Fig. 382), like the twelfth, is a centrifugal or motor nerve trunk. Its fibres arise from the nerve cells of the *ventral horns* of the six upper cervical segments and, in the lower part of the medulla, from that detached portion of the ventral horns which forms the so-called *lateral nucleus*.

Its central neurones probably reach these nuclei after the same manner as those of the spinal nerves. Its peripheral neurones take origin from the large cells of these nuclei, leave the grey matter at the dorso-lateral angle of the ventral horns, pass lateralward through the white matter, and make their exit from the lateral surface of the spinal cord and medulla in a vertical plane midway between the ventral and dorsal nerve roots of the spinal cord. Outside of the central nervous system they form small root bundles, which pass cephalad and unite to form the spinal accessory nerve trunk.

The tenth, pneumogastric, or vagus nerve (Figs. 383 and 384) contains both centrifugal and centripetal fibres. The neuraxes of its centrifugal or motor fibres arise from the large scattered nerve cells of the nucleus ambiguus, which are homologous with the more caudad group forming the lateral nucleus, and also with the nerve cells of the ventral horns of the spinal cord.

The neuraxes from the scattered cells of the *nucleus ambiguus* pass at first dorsalward until they reach the neighborhood of the tractus solitarius, where they join the centripetal bundles, pass lateralward and slightly ventralward, and make their exit from the side of the medulla just ventral to the margin of the restiform body. Outside of the medulla the several bundles unite to form the median portion of the vagus.

The central motor neurones of the vagus reach the medulla oblongata through the pyramidal tracts, and, having arrived at the proper level, turn dorsalward along the median raphé—in which they promptly decussate—and terminate by arborization about the cells of the nucleus ambiguus.

The peripheral neurones of the centripetal or sensory portion of the vagus, whose cell bodies lie in the *jugular ganglion*, enter the medulla along with its motor fibres. They pass inward toward the dorsal grey matter, at the border of which each fibre divides into a short ascending and a long descending branch. The long descending branches collectively form a small compact bundle of medullated fibres, the *tractus solitarius* (*fasciculus solitarius*, *tractus spinalis nervi vagi*). The fibres of this tract, after passing caudad for a considerable distance, terminate about a group of small nerve cells in the grey matter which surrounds the fasciculus, the *nucleus of the solitary tract*. The cells of this nucleus acting as neurones of the second order send their fibres, after the manner of the internal arcuates, to join the mesial fillet of the opposite side.

The short ascending branches, together with many collaterals from the descending processes, terminate about the small nerve cells of the *triangular* or *chief vagus nucleus* in the floor of the fourth ventricle. The cells of this nucleus, also acting as neurones of the second order, send their neuraxes, in a manner similar to those coming from the nucleus of the solitary tract, to the opposite mesial fillet, and are continued through neurones of higher orders to the cerebral cortex.*

The ninth or glossopharyngeal nerve (Figs. 383 and 384).—The course of the neuraxes of this nerve is exactly similar to those of the vagus. Its peripheral motor nerves begin as nerve cells of the cephalic end of the *nucleus ambiguus*, those belonging to the glossopharyngeal nerve not being in any way distinguishable from those of the vagus except by their superior position. Their neuraxes pass dorsalward to meet the incoming sensory neurones, in company with which they make their exit through the small lateral columns of the medulla oblongata.

The central motor neurones from the cerebral cortex arrive in the nucleus ambiguus after traversing the corona radiata, internal capsule, and pyramidal tracts; they then decussate in the median raphé, to terminate in arborizations about the nerve cells of the opposite side in the same manner as do the central neurones of the vagus path.

The peripheral sensory (centripetal) neurones of the glossopharyngeus begin as cell bodies in the *petrosal ganglion*, which, like the other root ganglia of the cranial nerves, is homologous with

* For the course of the mesial fillet, see page 531.

the dorsal root ganglia of the spinal nerves. Thus, the nerve cells of the petrosal ganglion send one process peripheralward, while the other enters the medulla through the sensory portion of the glossopharyngeal nerve roots. These fibres pass toward the dorsal grey matter and divide into a long ascending and a short descending branch. The former enters the *tractus solitarius* and ends about the adjacent cells of its nucleus in the manner already described for the vagus nerve. The latter, with some collaterals from the descending branches, passes to the *triangular* or *chief nucleus* of the glossopharyngeus just above but continuous with the similar nucleus of the vagus, in the floor of the fourth ventricle. From both of these nuclei new neurones of the second order continue the path cerebralward, decussating as internal arcuate fibres to enter the mesial fillet of the opposite side.

The glossopharyngeal roots are peculiar as compared with those of the vagus in that the root fibres of the former form finer bundles in their passage through the lateral columns to reach their sensory nuclei; also in the fact that the glossopharyngeus distributes the larger part of its fibres to the tractus solitarius, while the vagus sends the larger portion to the triangular or chief sensory nucleus.

The intermediate nerve of Wrisberg has its peripheral neurone cells in the *geniculate ganglion* of the facial nerve. Their central processes on entering the medulla pass to the *tractus solitarius* to terminate after the same manner as the similar fibres of the glossopharyngeus. Its fibres thus form the most cephalic portion of the solitary tract, the more caudad portions of the bundle being formed from fibres of the glossopharyngeus and vagus, respectively.

The eighth or auditory nerve (Figs. 384, 385, and 386), centripetal in direction, consists of two distinct divisions which differ in origin, distribution, and function. These are the *pars cochlearis* (*cochlear nerve, true auditory nerve*) and the *pars vestibularis* (*vestibular nerve*).

The peripheral neurones of the **vestibular nerve** arise from the nerve cells of the *ganglion vestibulare* (*ganglion of Scarpa*) in the internal auditory meatus. They enter the medulla oblongata at the lower margin of the pons and in the same vertical plane as the ninth and tenth cranial nerves. On approaching the grey matter in the floor of the fourth ventricle these neuraxes divide into a short ascending and a long descending branch.

The terminals of these fibres, together with those of their collaterals, end in one of several cell groups. 1. A large number end

about the cells of the *mesial* or *chief nucleus*, a large area in the floor of the fourth ventricle containing small scattered nerve cells; it is comparable to the chief nuclei of the ninth and tenth nerves. 2. Other fibres, probably for the most part ascending branches, pass to the *superior vestibular nucleus* (*von Bechterew's nucleus*), which is situated in a more dorsal and lateral plane and somewhat cephalad, from the mesial nucleus. 3. Other fibres end about the large cells of the *lateral vestibular nucleus* (*Deiters' nucleus*). 4. Still other fibres, mostly descending branches, pass caudad, as the *descending* or *spinal root of the vestibular nerve*, which passes down the medulla in the restiform body, following a course parallel, but lateral, to the tractus solitarius. The fibres of the spinal root end in relation to the nerve cells of the adjacent grey matter.

From the nerve cells of the descending root, as well as from the median and superior nucleus, neurones of the second order send their neuraxes as internal arcuate fibres to the fillet of the opposite side, through which they are continued toward the cerebrum.

Neurones of the second order, which include the cells of Deiters' nucleus, send their neuraxes caudad in a fairly compact bundle, which finally joins the fasciculus sulco-marginalis of the spinal cord, as already described. .

The vestibular nerve is also directly connected with the cerebellum by paths which can only be followed with considerable difficulty. Some neurones from the superior vestibular nucleus (*von Bechterew's*) are thought to enter the cerebellum through the superior peduncles. This group may, however, also contain peripheral neurones which pass without interruption to the vermis cerebelli. A second bundle enters the cerebellum through the corpus restiforme and is probably derived from the cells of Deiters' nucleus.

The cochlear nerve, the path of the acoustic impulses, contains neurones which begin as the bipolar nerve cells of the *ganglion spirale* in the internal ear. The distal processes of these cells are distributed to Corti's organ, their proximal branches collectively form the root of the cochlear nerve.

This nerve enters the medulla oblongata at the caudal margin of the pons, along with, but somewhat dorsal to the vestibular nerve. Near its entrance it passes into the *cochlear nucleus*, which it thus divides into a dorso-lateral portion (*dorsal cochlear nucleus* or *tuberculum acousticum*) and a ventro-mesial portion (*acoustic nucleus*, *ventral* or *chief cochlear nucleus*). Its fibres divide into

ascending and descending branches in the usual manner, and most if not all of them terminate in one of these two nuclei. A few fibres, however, are undoubtedly continued past the cochlear nuclei without interruption. The ventral cochlear nucleus probably receives the unusually short ascending branches, while most of the descending branches end in the tuberculum acusticum, which is continued spinalward for a considerable distance.

From the ventral nucleus neurones of the second order send their neuraxes in a ventro-mesial and somewhat cephalad direction to collectively form the *trapezoid body*, a compact fibre bundle which decussates behind the mesial fillet and enters the *superior olivary nucleus* of the opposite side. This nucleus is closely applied to the dorsal surface of the trapezoid body.

The neurones of the second order which arise in the dorsal cochlear nucleus or tuberculum acusticum, reach the opposite superior olive by a more circuitous route. They first pass dorsalward to the lateral margin of the floor of the fourth ventricle; in this grey matter they turn toward the median line, forming superficial coarse groups, the *striæ acusticæ*, which appear as macroscopic transverse ridges in the ventricular floor. At the lateral margin of the abducens these fibre bundles suddenly dip into the substance of the pons, pass ventral to the nucleus of the sixth nerve, decussate through the median raphé, and reach the opposite *superior olivary body* in which most of these fibres terminate.

Some fibres from the tuberculum acusticum and *striæ acusticæ*, as also some from the mesial nucleus and trapezoid body, are continued past the superior olives and enter the *lateral fillet* without interruption. The lateral fillet, however, consists chiefly of neurones of the third order, which arise in the superior olive of the same side. This tract is continued cephalad, lying at first near the lateral margin of the tegmental portion of the pons and dorso-lateral from the mesial fillet. The lateral fillet soon blends with the lateral margin of the mesial fillet to form a continuous sheet of longitudinal fibres. In the mesencephalon some at least of the neurones from the lateral fillet are interrupted at the *inferior corpora quadrigemina*, their neuraxes terminating by arborization about the scattered nerve cells of these bodies. From this point the auditory path is continued cerebralward by fibres which probably accompany the mesial fillet.

The seventh or facial nerve (Figs. 385, 386, and 387).—The peripheral neurones of this nerve, which in man is a purely centri-

fugal or motor nerve, begin in the nerve cells of the *facial nucleus*, a small oval group of large motor cells placed on the dorsal side of the trapezoid body, just dorso-lateral from the superior olive. Their neuraxes soon collect into a compact tract, which, in its first portion, passes dorsalward in the region of the abducens nucleus, around which it makes a sharp turn, the *internal genu*. It then passes somewhat cephalad, and finally takes a lateral, yet slightly ventral and caudad course, toward its exit at the lower margin of the pons Varolii, just dorsal to the root of the auditory nerve.

The facial tract thus presents three portions: (a) the proximal, whose direction is dorso-mesial and slightly cephalad; (b), the internal genu, whose course is first dorso-mesial and cephalad, but later ventro-lateral and cephalad, and (c) the distal, which is directed lateralward, but slightly ventralward, and caudad.

The central neurones of the facial reach its nucleus in the pons through the pyramidal tracts, probably by passing dorsalward along the median raphé, until at a point dorsal to the trapezoid body, where they decussate and pass directly to the facial nucleus.

The sixth or abducens nerve (Figs. 385 and 386) is entirely centrifugal or motor. Its peripheral neurones arise from the cells of the compact ovoid *abducens nucleus* which lies beneath the grey matter of the floor of the fourth ventricle on either side of the median line. It is in close relation to the fasciculus longitudinalis posterior, which lies on its ventro-mesial side, and with the tract of the facial nerve whose internal genu encircles the dorso-mesial angle of the abducens nucleus.

The neuraxes of the large nerve cells of this nucleus form bundles of considerable size, which pass almost directly ventralward, through the tegmentum and crusta of the pons, and emerge at the inferior margin of the rhombencephalon near the median line, where they unite to form the trunk of the abducens nerve.

The central neurones of the sixth nerve are derived from the pyramidal tracts. Having reached the pons Varolii, they pass dorsalward along the median raphé until near the abducens nucleus, where they decussate and immediately end about the nerve cells of the peripheral neurones.

The fifth or trigeminus nerve (*trifacial nerve*) (Fig. 387) contains a large sensory or centripetal, and a smaller motor or centrifugal root. Both make their entrance or exit at the lateral surface of the pons Varolii, plunging together into the substance of the middle cerebellar peduncles to reach the dorsal half of the tegmen-

tum in the mid-region of the pons Varolii. **The motor root** occupies a slightly cephalad position as compared with the sensory. Though the path of the central neurones which supply this root is not definitely known, from analogy it is reasonable to suppose that from the motor cortex their fibres start down the pyramidal tracts, as in the case of the central motor neurones of the other cranial nerves, but unlike these, they leave the pyramidal tracts at a level considerably cephalad from the nerve trunk for which they are destined. They probably decussate through the median raphé, and many of them then end about the nerve cells of the *substantia ferruginea* or *locus ceruleus* (*nuclei minores nervi trigemini*), a scattered group of large cells lying near the median line and ventral to the grey matter surrounding the aqueduct of Sylvius.

Some of the central motor neurones, however, are continued past this nucleus without interruption (*Vs*, Fig. 387, and *Vc*, Fig. 414), and these fibres, together with the neuraxes from the cells of the *substantia ferruginea*, pass caudalward as the *descending* or *mesencephalic root of the trigeminus*. This root above the trochlear decussation is lateral to the descending root of the fourth or trochlear nerve. Caudad to the trochlear decussation it is continued downward in the same plane and is thus found just dorso-lateral to the *substantia ferruginea* and resting upon the ventral surface of the grey matter which surrounds the aqueduct and forms the floor of the fourth ventricle.

At the level of the fifth nerve its mesencephalic root turns lateralward, many of its neuraxes (probably those coming from the cells of the *substantia ferruginea*) entering the motor root, and passing between the bundles of transverse pons fibres to their exit in the *portio minor* of the *trigeminus*. Other fibres of the descending root of the fifth (probably those central neurones which come from above the *locus ceruleus*) terminate in the *motor nucleus of the trigeminus* (*chief motor nucleus, nucleus princeps nervi trigemini*), a group of large nerve cells in the dorso-lateral part of the pontal tegmentum. This motor nucleus is ventro-mesial from the chief sensory nucleus and the incoming centripetal root (sensory root, *portio major*) of the *trigeminus*.

The nerve cells of the chief motor trigeminal nucleus are enveloped by an intricate network of collaterals derived from the neurones of the pyramidal tracts and of the minor trigeminal nuclei. The neuraxes of the cells of the chief nucleus, together with those from the cells of the *locus ceruleus*, form the motor root

of the trigeminus, and through this nerve trunk are distributed to the muscles of mastication.

The sensory root of the trigeminus, larger than the motor, enters the lateral portion of the pons Varolii slightly caudad to the motor root. Its fibres pass in a dorso-lateral direction until near the grey matter, where they divide into very short ascending and very long descending bundles. The latter form the long *spinal root of the trigeminus*, which is continued downward on the inner side of the restiform body to the cervical region of the spinal cord. Its fibres and collaterals successively end about the small nerve cells contained in the adjacent *substantia gelatinosa of Rolando*, which is continued upward from the tips of the dorsal horns in the spinal cord. The neuraxes of these cells—sensory trigeminal neurones of the second order—decussate as internal arcuate fibres and pass cerebralward in the mesial fillet.

The short ascending branches, together with many collaterals from the descending divisions, end in the *chief sensory nucleus* of the trigeminus, which begins in the extreme lateral portion of the pontal grey matter somewhat cephalad from the trigeminal root, and by a tapering extremity is continued spinalward as far as the gelatinous substance of Rolando in the medulla oblongata, with which portion of the grey matter it appears to be continuous.

The path of the central neurones from this nucleus is still uncertain. They probably pass, after the manner of the internal arcuate fibres, to the mesial fillet of the opposite side.

The Fourth or Trochlear Nerve (Figs. 388 and 389).—The peripheral neurones of the trochlear nerve begin in the large motor nerve cells of the *trochlear nucleus*, which lies in the grey matter between the aqueduct of Sylvius and the posterior longitudinal fasciculus at the level of the cephalic border of the inferior corpora quadrigemina and the decussation of the superior cerebellar peduncles. The nucleus comprises a compact group of large stichochrome nerve cells, which are in close relation to the dorsal surface and lateral margin of the posterior longitudinal fasciculus. These nuclei are characteristically asymmetrical in size, shape, and position.

From the nerve cells of this nucleus neuraxes pass spinalward in a small compact bundle lying in the ventro-lateral angle of the grey matter surrounding the aqueduct. This *descending root of the trochlear nerve* is placed dorso-mesial to the descending or mesencephalic root of the fifth nerve, and dorso-lateral to the posterior longitudinal fasciculus.

At the level of the spinal border of the inferior corpora quadrigemina and isthmus rhombencephali the root of the fourth nerve makes a sharp dorsal turn, passes around the lateral margin of the grey matter to its dorsal surface, where it enters the anterior medullary velum, decussates with its fellow of the opposite side, and makes its exit from the dorsal surface.

The fourth nerve is peculiar in that it is the only cranial nerve to leave the dorsal surface of the central nervous system, and is possibly the only one whose decussation is on the distal side of the trophic center for its peripheral neurones. It is also the only cranial nerve whose decussation is dorsal to the axial central canal.

As to the manner in which the central motor neurones reach the trochlear nucleus but little is known. We should, however, expect to find no decussation in the paths of the central neurones to this nerve. The trochlear nucleus is known to receive fibres from the region of the posterior longitudinal fasciculus, but whether these are central motor neurones or collaterals from the other ocular paths is at present uncertain. The latter deduction would appear to be the more probable.

The Third or Oculomotor Nerves (Figs. 390 and 413).—The nuclei of the oculomotor nerves form a series of cell groups in the mesencephalon. They lie in the grey matter between the aqueduct of Sylvius and the posterior longitudinal fasciculus and occupy the deep median trough which is formed by these fasciculi.

The nuclei of the oculomotorius include a median cell group (*median nucleus, nucleus impar*) which is also the most ventral portion, and a lateral group on either side of the median line which has been variously subdivided by different observers. It may be said to contain a ventro-medio-anterior nucleus (*the Westphal-Edinger nucleus*) and a dorso-latero-posterior portion (*ventral and dorsal lateral nuclei*).

The nerve fibres coming from the anterior two-thirds of the group of oculomotor nuclei are uncrossed, but those from the posterior or spinal third decussate to the opposite side and enter the lateral fasciculi of the oculomotor nerve roots. The root bundles from the various nuclei of the third nerve pass ventralward through the posterior longitudinal fasciculus, and through or around the red nucleus, to converge to a point near the median line; they make their exit at the *posterior perforated space*.

The course of the central neurones of the oculomotor nerves is not yet known. The nuclei of these nerves are closely connected

with each other and with the *posterior longitudinal fasciculus*. Through this fasciculus they are placed in intimate relation with the ocular centers of the lower cranial nerves.

The second or optic nerves differ markedly in their arrangement from the lower cranial nerves. From the standpoint of embryology and comparative anatomy the retina of the eye represents, in part,



FIG. 413.—A SECTION OF THE HUMAN BRAIN STEM, AT THE LEVEL OF THE SUPERIOR CORPORA QUADRIGEMINA.

Aq, aqueductus Fallopii; *Brqa*, arm of the anterior corpora quadrigemina; *Brqp*, arm or peduncle of the inferior corpora quadrigemina; *Cyl*, lateral geniculate body; *Cgm*, mesial geniculate body; *Cgma*, accessory nucleus of same; *Coqa*, commissure of the superior corpora quadrigemina; *Fcp*, bundle to the posterior commissure; *Ffp*, posterior longitudinal bundle; *Fpl*, lateral pontine bundle; *Fpr*, predorsal bundle; *GI*, *GII*, and *GIII*, superficial, middle, and deep grey layer; *Gml*, lateral ganglion of the mid brain; *III*, oculomotor nerve; *IIl*, lateral bundle of the tegmentum; *Lm*, lateral lemniscus; *Lmp*, bundle from the fillet to the crusta; *Nltg'*, accessory dorsal nucleus of the tegmentum; *NIII*, lateral oculomotor nucleus; *NIIIm*, mesial oculomotor nucleus; *NQa*, nucleus of the anterior corpora quadrigemina; *Pem*, peduncle of the mammillary body; *Pp*, crusta; *Pul*, pulvinar; *SnS*, substantia nigra; *Stri*, intermediate layer; *Strl*, layer of the fillet; *Stro*, layer of the optic nerve; *Strz'*, stratum zonale of the corpora quadrigemina; *tM*, deep medullary layer; *Trs*, rubro-spinal tract; *Tst*, spino-tectal and thalamic tract; *Vc*, cerebral root of the trigeminus. Weigert's stain. $\times 2$. (After Marburg.)

at least, a detached portion of the cerebrum. The optic nerves are therefore properly considered as *central* paths or tracts, and as such must contain sensory neurones of the higher orders.

Adopting this view, the true peripheral ganglion of the optic nerve would be formed by the inner nuclear layer of the retina

(*ganglion retinæ*). The bipolar cells of this layer form the peripheral neurones of the optic path. Their distal processes terminate in relation with the rods and cones; their central processes are continued into the optic nerve either, as possibly occurs, with-

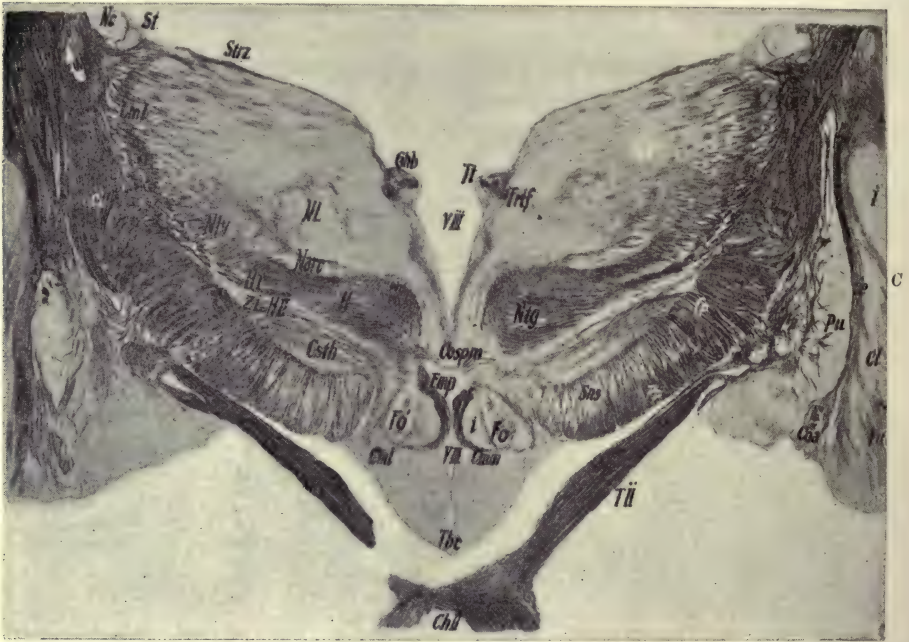


FIG. 414.—A SECTION OF THE HUMAN BRAIN STEM, AT THE LEVEL OF THE OPTIC CHIASM.

C, capsula extrema; *Ce*, external capsule; *ChII*, optic chiasm; *Ci*, internal capsule; *Cl*, claustrum; *Cml*, lateral nucleus of the mammillary body; *Cmm*, medial nucleus of same; *Coa*, anterior commissure; *Cospm*, supramammillary commissure; *Csth*, hypothalamic body of Luys; *Fmp*, principal fasciculus of the mammillary body; *Fo*, fornix; *fp*, perforating fibres of the crusta; *Frtf*, Meynert's bundle; *Fu*, uncinate fasciculus; *Ghb*, ganglion habenulæ; *H*, Forel's field; *HI*, dorsal part of same; *HII*, ventral part of same; *i*, internal nucleus of the medial ganglion of the mammillary body; *J*, internal nucleus of the medial ganglion of the mammillary body; *Narc*, arcuate nucleus; *Nc*, caudate nucleus; *NL*, centre médian; *Nlv*, ventro-lateral nucleus of the thalamus; *Ntg*, red nucleus; *Pp*, crusta; *SnS*, substantia nigra; *St*, stria cornea; *Strz*, stratum zonale of the corpora quadrigemina; *Tbc*, tuber cinereum; *TII*, optic tract; *Tt*, tænia thalami; *V III*, third ventricle; *Zi*, zona incerta. Weigert's stain. $\times 1\frac{1}{2}$. (After Marburg.)

out interruption, or, as is usually the case, by the interposition of a new set of neurones whose nerve cells form the large ganglion cell layer of the retina (*ganglion nervi optici*). Neuraxes from these large nerve cells (optic neurones of the second order) penetrate the nerve fibre layer of the retina, enter the optic nerve, decussate in

part in the optic chiasm—those coming from the internal portions of the retina decussate, those from the external portions pass the chiasm without crossing—and continue cerebralward through the optic tracts, which pass around the crura cerebri to enter the diencephalon (Figs. 391 and 414).

Some of these fibres terminate at once in the *lateral geniculate* body; a few are continued to the anterior corpora quadrigemina from which they are connected by intermediate neurones with the lower groups of motor ocular nuclei and with the cervical region of the spinal cord. Still other fibres of the optic tracts, together with those neurones of higher orders whose nerve cells lie in the lateral geniculate body, pass to the *pulvinar* of the optic thalamus, and are probably continued thence by neurones of a higher order through the optic radiation to the cortex of the occipital lobes.

The Olfactory Nerve.—

The peripheral neurones of the first or olfactory nerve include those nerve cells, *the olfactory cells*, which are found in the olfactory mucous membrane,* whose distal processes or dendrites

reach the free surface of the mucosa, and whose central processes, the neuraxes, pass, as non-medullated nerve fibres of the olfactory

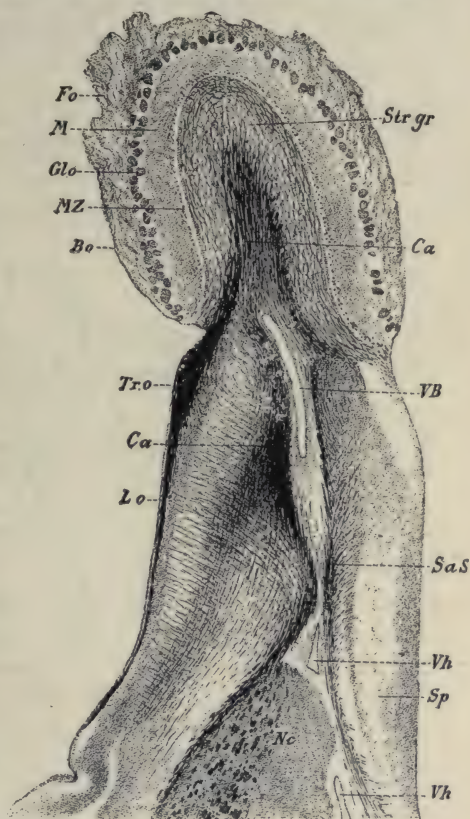


FIG. 415.—OLFACTORY LOBE AND BULB OF A RABBIT; HORIZONTAL SECTION.

Bo, olfactory bulb; Ca, anterior commissure; Fo, olfactory fibres; Glo, olfactory glomeruli; Lo, olfactory lobe; M, molecular layer of the olfactory bulb; NZ, mitral cells; Nc, caudate nucleus; SaS, white matter of the septum; Sp, septum pellucidum; Str gr, granular layer; Tr.o, lateral olfactory tract; VB, ventricle of the bulb; Vh, anterior horn of the lateral ventricle. Weigert's stain. (After Kölliker.)

* See Chapter XIV.

nerve, to the *olfactory bulb*, in which they terminate by end-arborizations that interlace with the dendrites of the *mitral olfactory cells* to form the so-called *olfactory glomeruli*.

The neuraxes of the large mitral cells of the olfactory bulbs (olfactory neurones of the second order) are continued as the olfac-

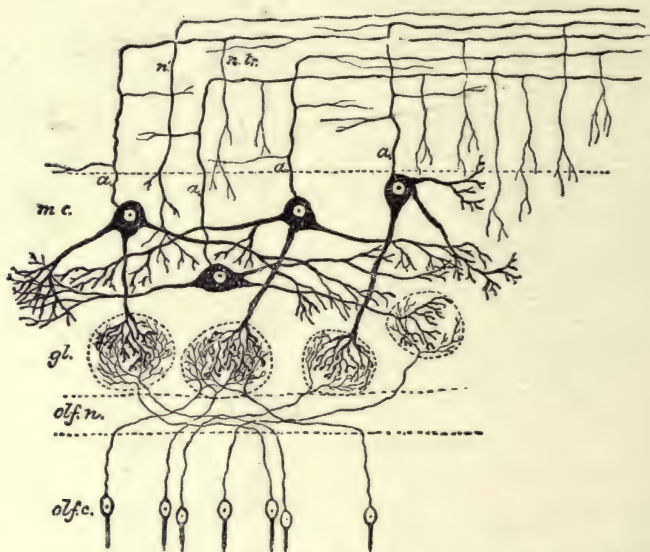


FIG. 416.—DIAGRAM OF THE RELATIONS OF THE NEURONES OF THE OLFACTORY NERVE AND OLFACTORY BULB.

olf. c., olfactory nerve cells, located in the olfactory region of the nasal mucosa, whose neuraxes enter the olfactory nerve *olf. n.*, and terminate in relation with the dendrites of the mitral cells, *mc.*, in the olfactory glomeruli, *gl.* The neuraxes of the mitral cells, *a.*, enter the olfactory tract, where they make a sharp bend and pass toward the cerebrum giving off frequent collaterals. At *n'* a nerve fibre appears to end by a free ramification among the mitral cells of the olfactory bulb. (After Schäfer.)

tory tracts through the medullary center of the bulbs. The central terminals of these fibres are distributed in many directions and are only followed with great difficulty.

Some of these fibres enter the anterior commissure and decussate to the opposite side; others enter the columns of the *fornix* and pass directly to the *hippocampus*. Still others pass to the *mammillary bodies* and *uncinate gyrus* and are thence connected, by neurones of higher orders, with the hippocampus. These latter fibres are possibly also connected by fibre tracts with the small *ganglion interpedunculare* near the ventral surface of the diencephalon, with the *ganglion habenulæ* near its dorsal surface, and with the *optic thalamus*.

CHAPTER XXVII

THE NERVOUS SYSTEM (*Continued*)

E. THE MENINGES AND BLOOD SUPPLY

THE brain and spinal cord are enveloped by the meninges, which include three fairly distinct membranes, the dura mater, arachnoid, and pia mater, and two cavities filled with lymph or a lymph-like fluid; by this arrangement the cerebro-spinal axis is, as it were, suspended in fluid, and is everywhere surrounded by a watery cushion.

The dura mater is the outermost of the three coats. Within the cranial cavity it is firmly attached to the bony walls, and serves as a periosteum for the internal surface of the bones which form the cranial cavity. Within the medullary cavity of the spinal cord the dura mater is distinct from the periosteum of the vertebræ, with which it is connected by loose fibrous tissue and masses of fat, which inclose large lymphatic spaces or chambers, lined by endothelium and collectively forming the *epidural space*.

The dura mater is composed of interlacing bundles of fibrous tissue containing few elastic fibres. The disposition of its fibre bundles varies somewhat in its different portions. In its spinal portion, most of the bundles are longitudinally disposed, comparatively few passing circularly around the circumference of the spinal canal; within the cranial vault the bundles cross at acute angles; in the falces and in the tentorium cerebelli they are radially disposed.

The cranial dura consists of two distinct layers, an outer, which is very vascular and serves as the bony periosteum, and an inner, which is but slightly vascular and may be considered as the *dura propria*. It is the inner layer only which is prolonged inward to form the falx cerebri and the falx and tentorium cerebelli. The venous sinuses of the cranium are inserted between the two layers of the dura.

Although the dura mater is but poorly supplied with blood vessels, it is relatively rich in lymphatics, which open into the subdural and epidural spaces and are continuous with the perivascular and perineural lymphatics which leave the cerebro-spinal cavities in company with the cranial and spinal nerves and the larger blood vessels. In this way the lymphatics of the dura mater and its adjacent spaces are in communication with the lymphatic vessels of the eye, nose, ear, and cervical lymphatic nodes. These communications are of special importance as indicating the path followed by certain pathological processes which involve the meninges.

Where the outer surface of the dura is not attached to the surrounding bone or connective tissue, it is covered by a thin endothelial coat, the lining endothelium of the epidural spaces. Its inner surface is lined by somewhat thicker endothelial cells, forming the wall of the *subdural space*.

The arachnoid is a thin membranous sheet which is suspended between the dura and the pia mater. It is composed of a delicate areolar tissue which contains relatively few elastic fibres and almost no blood vessels. This thin fibrous membrane is covered on either side by a layer of endothelium; that upon its outer surface consists of endothelial cells of considerable thickness, which are derived from the lining membrane of the inner wall of the subdural space; the cells upon its inner surface are thinner and are derived from the walls of the *subarachnoid space*.

Delicate septa-like bands pass from the inner surface of the arachnoid to the adjacent portions of the pia mater. These processes are likewise invested by the endothelial lining of the subarachnoid space. A similar investment clothes the processes of the *ligamentum dentatum* of the spinal cord which attaches the pia mater spinalis on either side to the adjacent portions of the dura mater.

A fibrous septum passing from the arachnoid to the pia mater, along a line opposite the posterior median fissure of the spinal cord, forms a fairly definite partition, the septum posticum. In the cervical region this is an uninterrupted septum, but in the thoracic and lumbar regions it is incomplete. The lymphatics of the arachnoid membrane communicate with those of the pia mater through this and other septa-like bands which unite the two membranes.

The cranial arachnoid, in the vicinity of the cranial sinuses, sends outward many villus-like projections or *arachnoid villi*

(*granulations arachnoidales*) which protrude into the venous sinuses to such an extent as often to produce corresponding depressions in the inner surface of the bones of the cranial vault, into which they push, carrying before them a much attenuated portion of the dura mater. These villi are similar in structure to the membranous portion of the arachnoid and are abundantly supplied with small blood vessels and lymphatics.

Fluid injected into these lymphatics or into the neighboring portions of the subarachnoid space passes readily into the lymphatic spaces of the dura mater, and may even be forced into the venous cavity of the cranial sinuses. While fluid thus injected may follow artificial rather than natural channels, it seems quite possible that the cerebro-spinal fluid may during life find its way along such channels into the venous sinuses to the relief of excessive intracranial pressure.

The pia mater is intimately adherent to the surface of the brain and spinal cord. It follows all the irregularities of their surfaces and sends prolongations into all their sulci. In the larger fissures these invaginations form a double fold of pial tissue; in the smaller, the invaginated portions fuse to form a thin septum-like prolongation of the pia. In this particular the pia mater differs from the arachnoid, which bridges over all the sulci without dipping into any but the largest fissures. It differs also from the dura mater which, with the exception of the falces and tentorium, is not prolonged into any of the fissures or sulci of either the brain or the spinal cord.

The pia mater is a connective tissue membrane and is divisible into an inner and an outer layer. The outer layer is composed of coarse fibrous bundles the most of which in the pia mater of the spinal cord run longitudinally, while the finer fibres of the thin inner layer are circularly disposed.

Between the two layers are many blood vessels and lymphatics, the pia mater being typically a vascular membrane. The larger blood vessels are loosely embedded in the outer surface of the pia, some of them projecting into or even lying entirely within the subarachnoid space. The outer surface of the pia mater, as also the sheaths of the vessels which are loosely attached to its surface, is covered with a layer of very thin endothelial cells derived from the lining membrane of the subarachnoid space.

The inner surface of the pia is everywhere firmly adherent to the surface of the brain and spinal cord. The slender trabeculae

and septa-like processes which extend into the superficial portions of these organs, consist of connective tissues whose fibrous bands are continuous with those of the membranous pia mater. In the spinal cord many of these fibrous bundles extend inward as far as the grey matter. In both the spinal cord and the brain the pial septa serve for the support of numerous blood vessels and perivascular lymphatics which are distributed through this connective tissue to all portions of the brain and spinal cord.

Within the cranium, reduplications of the pia mater, carrying between their folds a layer of arachnoidal tissue and an extensive plexus of small blood vessels, push their way into the cerebral ventricles to form the superior and inferior *telæ choroideæ*. These choroid plexuses are separated from the ventricular cavities by an investment of cuboidal cells, which in fetal and infantile life are ciliated, and which are derived from and are continuous with the *ependyma cells* lining the walls of the ventricles. Thus the blood vessels of the *telæ choroideæ*, in the strictest anatomical sense, lie without and not within the cavity of the cerebral ventricles, for they are everywhere separated from those cavities by the *ependyma cells*, which, ontogenetically at least, form a portion of the wall of these vesicles.

The peculiar arrangement of the three constituent membranes of the meninges leaves three distinct spaces or connected groups of spaces which are filled with fluid. These are the epidural, subdural, and subarachnoidal spaces.

The epidural space comprises a connected series of lymph cavities, which is of limited extent within the cranium, but of broad extent within the spinal canal. These spaces are lined by endothelium which is at many points continuous with the perivascular and perineural lymphatics and through them with the lymphatic vessels of the general systemic circulation. Obviously the epidural spaces serve as large lymphatic vessels and their cavities are consequently filled with lymph.

The subdural space has a complete lining of rather thick endothelial cells. The walls of this cavity are formed by the dura on the outer, and the arachnoid on the inner side. Its cavity is occupied by lymph and is continuous with the lymphatic vessels of the dura, and through them with the epidural spaces and systemic lymphatics.

This space is penetrated by the outgoing cranial and spinal nerves, which receive an investment from all three of the meningeal

coats. The three layers composing this investment soon lose their distinctive characteristics, fuse together, and blend with the epineurium of the nerve trunks.

Fluid injected into the subdural space may be readily forced into the lymphatics of these epi- and perineural sheaths and may thus travel to parts quite remote from the central nervous system.

The subarachnoid space within the cranium is of limited breadth, but within the spinal canal it is much broader and contains not only the larger blood vessels which are loosely attached to the surface of the pia, but also the many spinal nerve roots pass downward through this space toward their foramina of exit.

The subarachnoid space is lined by a thin endothelial layer, its outer wall being formed by the arachnoid, its inner by the outer surface of the pia mater; its cavity is filled with cerebro-spinal fluid, which closely resembles, yet differs somewhat in chemical composition from the lymph. This space is in communication through the foramen of Majendie with the central canal of the spinal cord and the ventricular cavities of the brain. It is also thought to communicate with the cerebral ventricles at several other points.

The spinal portion of the subarachnoid space is crossed by a posterior median septum, the septum posticum, laterally by the ligamentum dentatum, and by several irregular but incomplete septa which, like the ligamentum posticum, connect the pia mater with the arachnoid.

The ligamentum dentatum is a dense mass of fibrous tissue containing few elastic fibres, which, beginning at the lateral surface of the pia as a complete septum, passes, by about twenty-eight serrations, across the subarachnoid space, and pushing the arachnoid before it, is attached to the inner surface of the dura mater. The serrations of the dentate ligament do not penetrate the subdural space, for around the point of their attachment the surface of the arachnoid is firmly adherent to the dura mater. Each serration is invested by an endothelial coat continuous with the lining of the subarachnoid space.

Blood Supply.—The blood supply of the central nervous system is derived from vessels which lie within the folds of the pia mater. The larger arteries form an anterior longitudinal group represented in the spinal cord by the anterior spinal artery and its branches, and in the brain by the vessels of the circle of Willis and their immediate branches.

Two sets of vessels may be said to be distributed from these sources—one of which is distributed through the pia mater to the adjacent white matter of the spinal cord and to the grey pallium of the brain; the other penetrates the spinal cord through the anterior median fissure to be distributed to the central grey matter, and in the brain is represented by the branches of the middle cerebral arteries which penetrate directly to the ganglionic grey matter in the interior of the cerebrum.

In the spinal cord the vessels of the former set are mostly distributed to the white cortex, the larger branches, however, penetrate the white matter and aid in the formation of the capillary network of the grey medulla. In the brain their distribution is similar, the smaller pial vessels, *the cortical arteries*, being distributed to the cortex, which in this case is formed by the grey matter; the larger, *the medullary arteries*, penetrating to the white medulla in which they break up into capillary vessels.

The veins trend in the opposite direction and in the pia mater collect into large vessels, which in the brain open into the sinuses of the dura mater, and which in the spinal cord form the anterior and posterior median veins.

All of the larger vessels receive thin fibrous investments from the pia mater, the smaller vessels and capillaries are surrounded by neuroglia.

There are frequent anastomoses between the larger veins; the arteries, however, are all *terminal arteries* according to Cohnheim's classification, each artery possessing no anastomosis with the capillary areas of other vessels.

The more important facts concerning the ultimate distribution of the arterial branches are purely macroscopical, and for them the reader is referred to text-books on the general anatomy of the nervous system.

CHAPTER XXVIII

THE EYE

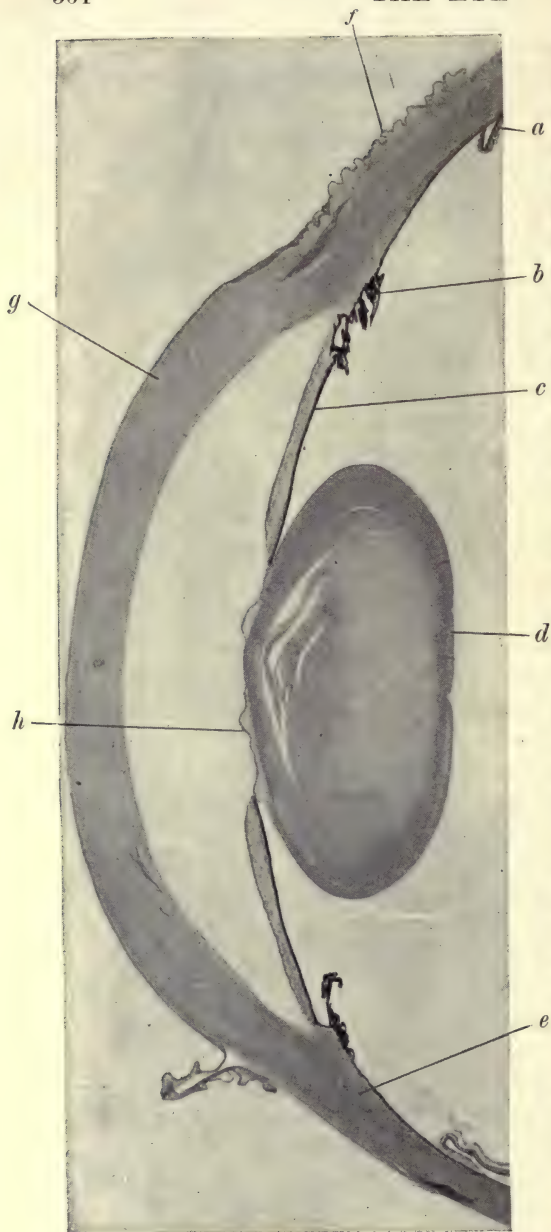
THE eye may be said to consist of the visual organ, or globe, together with its appendages—the eyelids, conjunctiva, and lachrymal apparatus—whose function is chiefly protective.

The globe of the eye, or eye proper, is contained within the cavity of the orbit, its posterior two-thirds being embedded in a mass of intraorbital fat whose inner surface is covered by a thin fibrous membrane or fascia which is clothed with endothelium. The endothelium is reflected from this fascia to the surface of the ocular globe, along a line just posterior to the border of the conjunctiva, whence it passes over the surface of the globe as far posteriorly as the optic nerve, on the surface of which it again becomes continuous with the endothelium of the fascia. Thus a serous sac or lymphatic space is formed by the parietal layer of this sac, which lines the orbital cavity, in conjunction with the visceral layer which covers the posterior two-thirds of the globe of the eye; this sac is the *capsule of Tenon*.

The anterior third of the globe is covered by the palpebral portion of the conjunctiva, which also clothes the inner surface of the eyelids, and at the fornix conjunctivæ is reflected upon the eyeball a little in front of its equator, whence it is continued forward, as the ocular or scleral conjunctiva, as far as the margin of the eye; here it becomes continuous with the anterior corneal epithelium.

The globe of the eye or *eyeball* is a spheroidal body whose surface consists of *three coats*, an outer, middle, and inner, and whose contents are the vitreous and aqueous humors and the crystalline lens.

The eyeball is not a true sphere, but may be said to comprise segments of two spheres, the smaller of which is inserted into the anterior surface of the larger. The anterior or smaller segment consists chiefly of transparent tissues which permit the entrance of light. Its border nearly corresponds to the posterior margin of the



ciliary body, and it may be approximately indicated by a parallel circle midway between the margin of the cornea and the equator of the eyeball. The anterior segment contains the cornea, the sclero-corneal junction, the anterior and posterior chambers, the aqueous humor, the iris, and the ciliary body. The posterior segment comprises the posterior two-thirds of the eyeball and includes the sclera, choroid, retina, and, within these coats, the vitreous humor. The crystalline lens with its suspensory ligament forms, as it were, a partition separating the two segments.

The optical or visual axis of the eye is a horizontal, antero-posterior, imaginary line which extends from the center of the cornea through the center of the anterior chamber, the center of the pupillary opening of the iris, the center of the crystalline lens, and the center of the

FIG. 417.—THE ANTERIOR SEGMENT OF A CHILD'S EYE; MERIDIONAL SECTION.

a, ora serrata; *b*, ciliary processes; *c*, iris; *d*, crystalline lens; *e*, ciliary muscle; *f*, ocular conjunctiva; *g*, cornea; *h*, the capsule of the lens, partially detached. Hematein and eosin. Photo. $\times 10$.

vitreous humor, and reaches the fovea centralis which lies in the middle of a thickened portion of the retina, the macula lutea.

Toward the inner side, at a distance of 3.5 mm., and about 1 mm. below the center of the fovea centralis, is the entrance of the optic nerve. This nerve pierces the coats of the eye, its fibres spreading out in a radial manner, upon the inner surface of the retina.

The extremities of the visual axis mark the two poles of the ocular globe; the anterior extremity, lying in the center of the cornea, is in the anterior or smaller spheroidal segment, the posterior extremity, in the fovea centralis, lies in the posterior segment of the eye.

THE EXTERNAL COAT

The outer tunic of the eyeball includes the cornea, the sclera, and the sclero-corneal junction.

THE CORNEA.—The cornea is a concavo-convex, transparent, colorless disk of approximately equal thickness throughout all its portions. It is nearly circular in outline, its horizontal exceeding its vertical diameter by only 0.5 mm.; its external surface is convex, its internal surface concave. The cornea forms the anterior one-fourth of the tunica externa, and represents a spheroidal segment whose radius is somewhat shorter than that of the posterior segment of the eyeball. It is inserted into the anterior margin of the sclera much after the manner in which a watch-glass is set in its rim; hence the inner surface of the cornea possesses a slightly greater diameter than the outer.

The cornea may be said to consist of *five layers*: 1, the anterior epithelium; 2, the anterior homogeneous membrane; 3, the corneal substance; 4, the posterior homogeneous membrane; 5, the posterior epithelium.

The anterior epithelium (*corneal epithelium, corneal conjunctiva*) at the margin of the cornea is continuous with the scleral portion of the conjunctiva. It consists of a relatively thin layer—six to eight cells deep—of stratified squamous epithelium, the deepest cells of which are elongated or columnar, the middle cells polyhedral, and the superficial cells somewhat flattened. The cells at all levels are nucleated and, like the other corneal tissues, perfectly transparent. The columnar cells are often slender and much elongated, their pointed apices extending well toward the surface of the epithelial layer.

The epithelium rests directly upon the anterior homogeneous layer. The deeper cells of the epithelium present distinct inter-

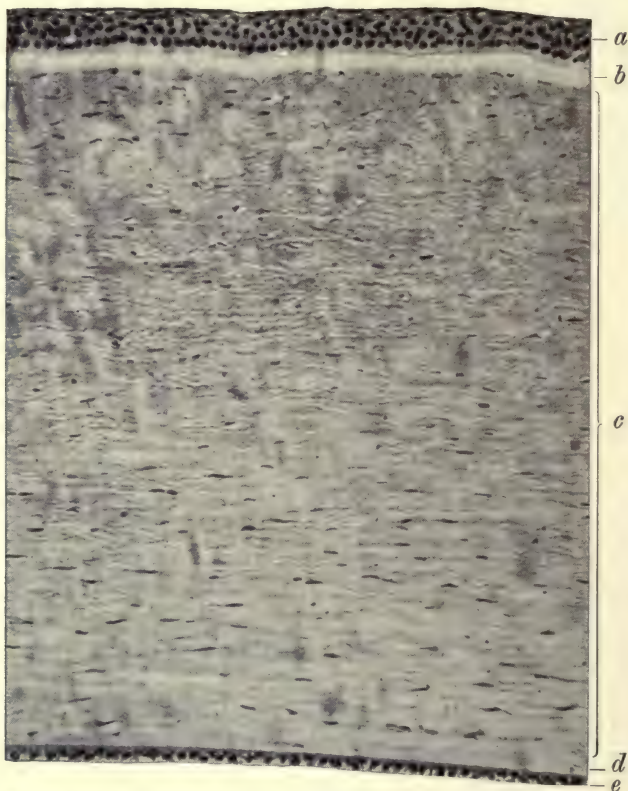


FIG. 418.—FROM A MERIDIONAL SECTION OF THE HUMAN CORNEA.

a, anterior corneal epithelium; *b*, anterior homogeneous membrane; *c*, substantia propria; *d*, posterior homogeneous membrane; *e*, posterior corneal epithelium. Hematein and eosin. Photo. $\times 180$.

cellular lymphatic spaces and intercellular bridges. Between the cells are the terminal ramifications of nerve fibrils from the plexus in the corneal substance.

The anterior homogeneous membrane (*anterior basal membrane, elastic membrane of Bowman*) was formerly thought to consist of elastic tissue, but this supposition is disproved by its ready solubility on boiling (His), as well as by the fact that it does not react typically to the specific stains for this tissue. Bowman's membrane is apparently a homogeneous or structureless coat except that

it is slightly fibrillar at its extreme margin where it becomes continuous with the fibrous tissue of the sclera. It resembles elastic tissue in that it is highly refractive and possesses a shining glassy appearance. It does not stain readily with the ordinary dyes.

The corneal substance (*substantia propria*) forms the greater portion of the cornea. It consists of a lamellated connective tissue, which forms about sixty fibrous layers, parallel to the corneal sur-

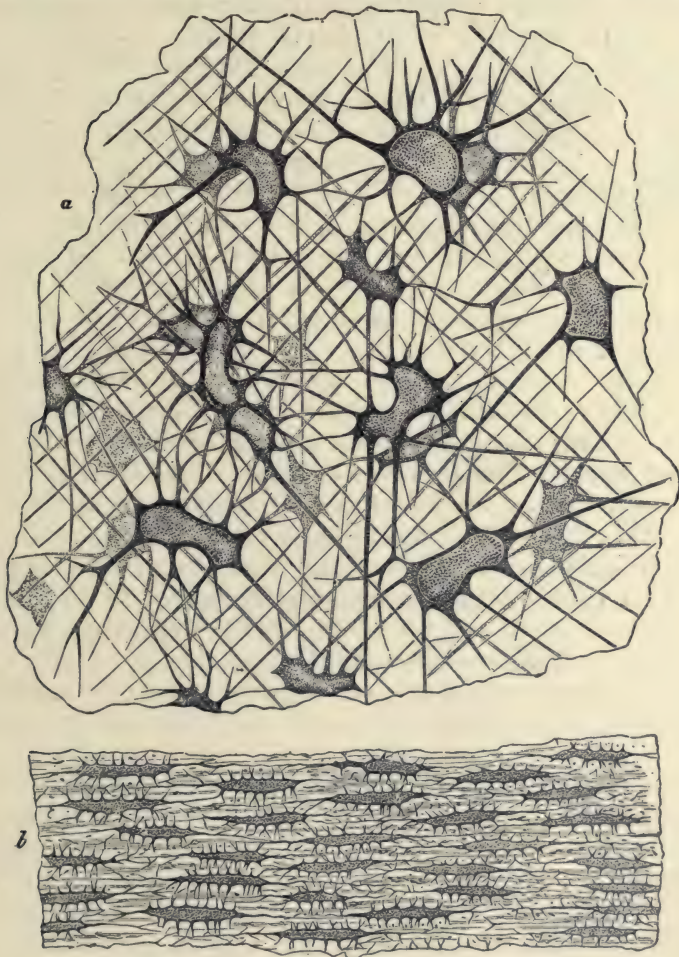


FIG. 419.—CORNEAL CORPUSCLES OF THE FROG.

a, as seen in tangential section; *b*, as seen in transection of the cornea. Chlorid of gold. Highly magnified. (After Rollett.)

face. The fibrous bundles of these lamellæ, being arranged in meridional curves parallel to the surface, appear to cross one another at right angles in the central portion of the circular cornea.

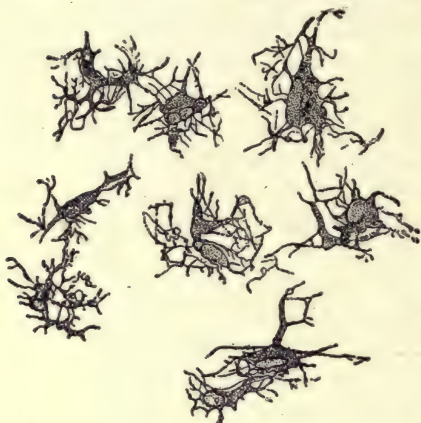


FIG. 420.—CORNEAL CORPUSCLES, ISOLATED.
Highly magnified. (After Waldeyer.)

Other fibres, arcuate fibres, pass from one layer to another; so firmly uniting them that it is impossible to tease the cornea into its component lamellæ.

The intervals between the fibrous layers are occupied by interlamellar, cement, or ground substance, in which lymphatic channels and large flattened cells, the *corneal corpuscles*, can be demonstrated. The corneal corpuscles are branched lamellar connective tissue cells, which occupy the large lymphatic

spaces or lacunæ of the interlamellar ground substance, and which send fibre-like processes into the interlacing lymphatic channels.

The posterior homogeneous membrane, or *membrane of Descemet* (*posterior basal membrane*), is similar in structure to the anterior. Like the latter, though formerly considered an elastic membrane it does not give the specific reactions of elastic tissue. It is somewhat thicker than Bowman's membrane. At its margin the membrane is continuous with fibrous bundles which are directed outward into the ligamentum pectinatum, and, at least in some animals, through this ligament into the ciliary margin of the iris. The membrane of Descemet can be readily detached from the corneal substance by teasing.

The posterior epithelial layer (*corneal endothelium*) consists of clear, cuboidal or flattened cells, placed edge to edge, and bound together by intercellular bridges. At the margin of the cornea it is reflected over the lateral wall of the anterior chamber to the anterior surface of the iris. Its cells rest upon the posterior homogeneous membrane.

All the tissues of the cornea, during life, are absolutely transparent. The elements of which they consist are of almost identical refractive indices, so that in very fresh, or in living tissue, it is

almost impossible for the microscope to discover any of the structure of the cornea. After death the cornea becomes opaque and its elements are then easily distinguished.

Vascular and Nerve Supply.—The cornea itself is an absolutely non-vascular tissue, having neither blood nor true lymphatic vessels. It is, however, well supplied with nerve fibres, derived from the ciliary nerves, which form an annular plexus in the sclera about the margin of the cornea, from which point bundles of naked axis-cylinders pass into the corneal substance to form a basal plexus near the anterior homogeneous membrane. From this latter plexus, fibres are distributed to the corneal substance and to a subepithelial plexus, anterior to Bowman's membrane, whence terminal fibrils penetrate the anterior epithelium.

THE SCLERA.—The sclera (*sclerotic coat*) is a firm opaque connective tissue membrane which forms the outermost layer of the posterior segment of the eyeball. It consists of two layers, the thick, firm, *substantia propria*, and the very thin, delicate, *lamina fusca*.

By reflected light the sclera of the adult is of a lustrous white color. In the child it has a faint bluish tint, due to the presence of pigment in the deeper layers of the child's eye which shows indistinctly through the relatively clear superficial tissues. The anterior portion of the sclera is covered by the conjunctiva and is familiarly known as the "white of the eye."

That portion of the sclera which is posterior to the ocular equator is covered by the visceral layer of the capsule of Tenon except at the insertions of the straight and oblique muscles. The tendons of these muscles pierce the capsule and are obliquely inserted into the surface of the sclera in a line nearly corresponding to the equator of the eye. The tendon bundles of the muscles are directly continuous with the fibrous bundles which compose the sclera.

The Substantia Propria.—The white fibrous tissue of the sclera is disposed in bundles which are arranged along meridional and equatorial lines; they interlace with one another to form a dense network. A few elastic fibres are interspersed among the bundles of this network.

The Lamina Fusca.—The inner surface of the sclera presents a fine gauzy membrane which can be readily detached by teasing. This is the *lamina fusca scleræ*. It consists of delicate interlacing fibrous bundles and numerous pigmented connective tissue cells.

The lamina fusca near the posterior pole is firmly adherent to the scleral substance.

At the posterior pole of the eye the sclera is pierced by the optic nerve, whose numerous bundles penetrate the coats of the eyeball and give to this portion of the sclera a cribrous appearance. This area of the sclerotic coat is known as the *lamina cribrosa scleræ*. It is a circular zone whose border is outlined by the entrance of the posterior ciliary arteries and the ciliary nerves. This is the thickest portion of the sclera, the coat becoming progressively thinner toward the equator of the eye; near its anterior margin it is again thickened by the tendinous insertions of the extrinsic muscles.

The sclera is chiefly supplied by branches from the posterior ciliary arteries, which form a wide-meshed plexus in its substance, its vessels anastomosing freely with those of the choroid coat.

The sclero-corneal junction (Fig. 422) is a narrow circular zone at the margin of the cornea, where it is inserted into the sclera. Across this narrow zone the fibrous bundles of the opaque sclera are continued directly into the similar, though perfectly transparent, bundles of the corneal substance.

The anterior or outer surface of this zone is covered by the ocular portion of the conjunctiva. Its epithelium is of the stratified squamous variety and is continuous with the anterior epithelium of the cornea.

From the inner surface of this junctional zone the anterior extremities of the muscle fibres composing the ciliary muscle take their origin. The fibres of this muscle intermingle with the marginal fibres of the posterior homogeneous layer of the cornea to form the *ligamentum pectinatum*, which connects the sclero-corneal junction with the base of the iris.

Toward the inner side of the scleral margin and near the border of the cornea is the *canal of Schlemm*. The nature and function of this canal are somewhat uncertain. It frequently contains blood cells, but also appears to be in direct communication with the numerous lymphatic *spaces of Fontana*, which lie in the lateral wall of the anterior chamber and between the fibre bundles of the *ligamentum pectinatum*. The spaces of Fontana are true lymphatic spaces and are in communication with the anterior chamber of the eye.

Blood Supply.—The sclero-corneal junction is abundantly supplied with blood from the anterior ciliary vessels, which, with the posterior conjunctival vessels, form loops at the margin of the cornea and anastomose freely with the vessels of the ciliary body.

THE MIDDLE COAT

The middle tunic (*uvea, uveal tract*) includes the choroid coat, ciliary body, and iris, together with an opening at the anterior pole of the eye, the pupil.

The iris divides the cavity of the anterior segment of the eye into an *anterior chamber*, included between it and the posterior or inner surface of the cornea, and a *posterior chamber*, which is bounded by the iris in front and the crystalline lens and its suspensory ligament behind. The free or pupillary margin of the iris is in light contact with the anterior surface of the lens. The posterior chamber is therefore an annular compartment.

THE CHOROID COAT.—The choroid coat (*tunica chorioidea*) consists of three layers: 1, the lamina suprachorioidea; 2, the lamina vascularis; 3, the lamina capillaris.

The lamina suprachorioidea (*suprachoroid layer*) is a very delicate membrane which contains many pigmented cells and is similar in structure to the lamina fusca of the sclera.

The flattened pigment cells are brownish-black in color from the many coarse granules which they contain, and are irregularly

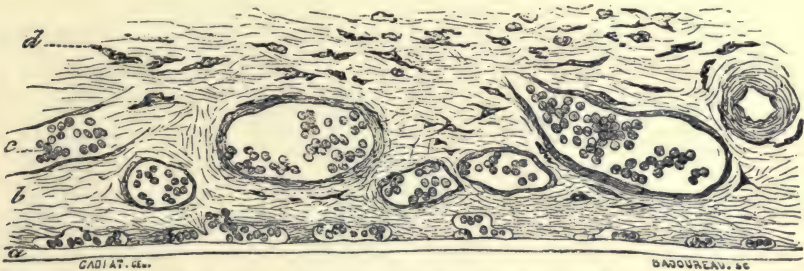


FIG. 421.—FROM A MERIDIONAL SECTION OF THE CHOROID COAT.

a, membrane of Bruch; *b*, the inner margin of the vascular layer. Between *a* and *b* is the capillary layer or chorio-capillaris; *c*, venule containing blood corpuscles; *d*, fibrous layer of the choroid or lamina suprachorioidea. Highly magnified. (After Cadiat.)

disposed, either separately or in groups. Lymphatic spaces occur between this layer and the sclera and communicate with the capsule of Tenon.

The fibres of this layer are not only distributed in its own plane but pass obliquely to the lamina fusca, thus loosely attaching the suprachoroid layer to the sclera. Similar, obliquely disposed fibres pass to the deeper portions of the choroid, with the fibres of which they blend.

The lamina vasculosa (*vascular layer, choroid proper*), so called because it contains the ramifications of the ciliary arteries and veins, is by far the thickest of the three layers of the choroid. It may be arbitrarily separated into an outer stratum, consisting chiefly of dense interlacing bundles of connective tissue fibres which inclose only the larger blood vessels, and an inner stratum of similar structure, but everywhere permeated by a close network of small vascular twigs. So dense is this network near the posterior pole of the eye, as to give the layer the appearance of an almost continuous sheath of small blood vessels.

The Lamina Capillaris.—Within the vascular layer is the capillary membrane (*lamina capillaris, lamina chorio-capillaris, tunica Ruyschiana*, which contains an exceedingly close-meshed capillary network. This network is specially dense near the macula lutea at the posterior pole of the eyeball. Its inner surface forms a very thin homogeneous membrane, the *lamina basalis* or *membrane of Bruch*, which increases somewhat in thickness as age advances. The inner surface of the lamina basalis is indented by the bases of the adjacent pigment cells of the retina. Anteriorly the vessels of the chorio-capillaris, like those of the vascular layer, become continuous with the vessels of the ciliary body and iris.

THE CILIARY BODY.—The ciliary body (*corpus ciliare*) represents the thickened anterior border of the choroid coat. It is, therefore, of annular shape and occupies a zone whose posterior border blends with the choroid at a point opposite the ora serrata of the retina, and whose anterior margin is continued into the iris opposite the sclero-corneal junction. It may be said to consist of three structures arranged in layers of varying thickness: 1, the *ciliary muscle*; 2, the *fibrous layer* with its *ciliary processes*; and 3, that portion of the pigmented epithelium of the retina which constitutes the *pars ciliaris retinae* or *ciliary epithelium*, and covers the inner surface of the ciliary body. The suspensory ligament of the crystalline lens is attached to the inner surface of the retinal epithelium.

The ciliary muscle consists of an annular mass of non-striated fibres which arise from the inner surface of the sclera near the sclero-corneal junction, and are inserted into the entire breadth of the fibrous mass of the ciliary body as far back as the anterior margin of the choroid. The muscle fibres are divisible into three sets, according to the direction of their long axis; these are the *meridional*, the *radial*, and the *circular*.

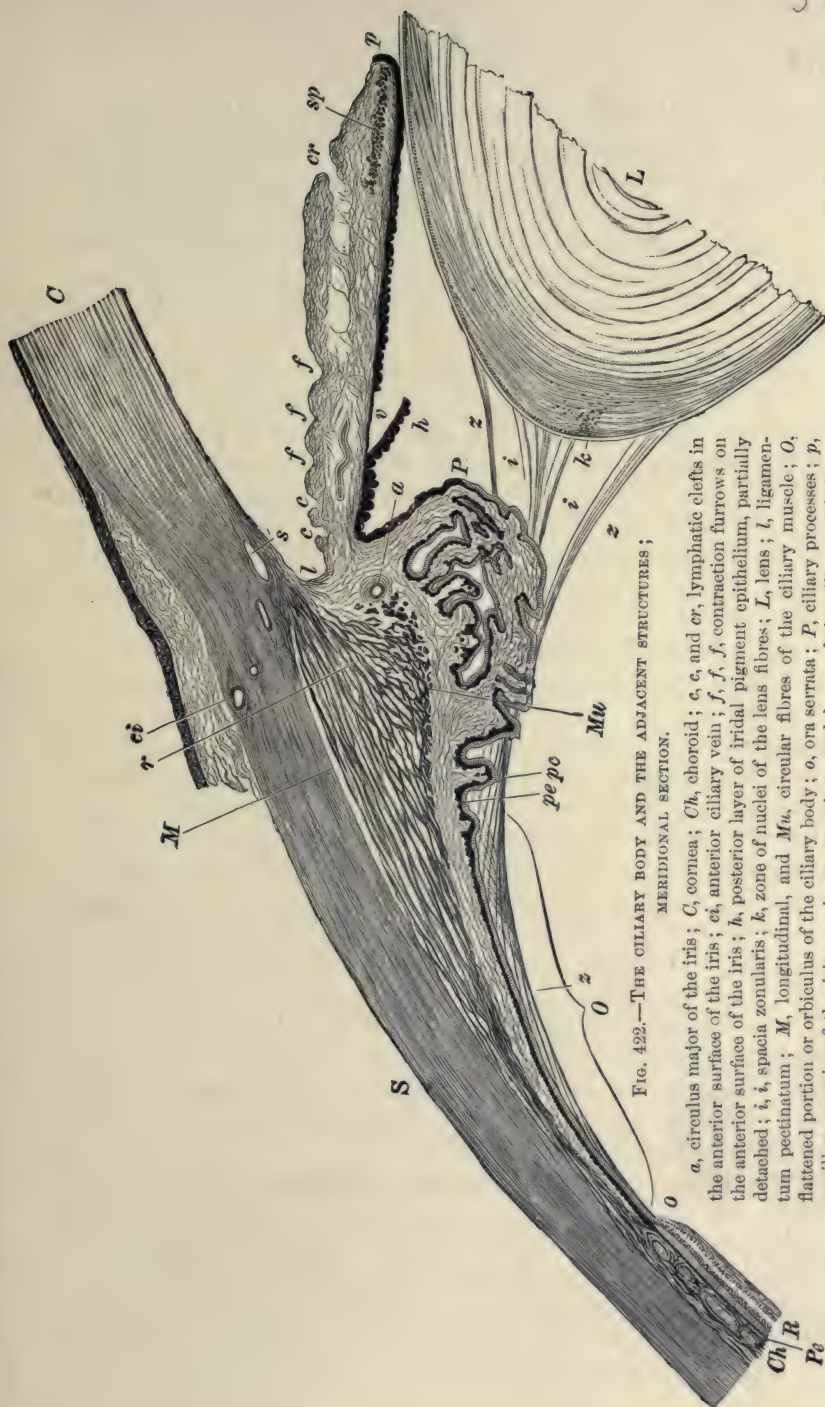


FIG. 422.—THE CILIARY BODY AND THE ADJACENT STRUCTURES;
MERIDIONAL SECTION.

a, circulus major of the iris; *C*, cornea; *Ch*, choroid; *a*, *c*, and *cr*, lymphatic clefts in the anterior surface of the iris; *ci*, anterior ciliary vein; *f*, *f*, contraction furrows on the anterior surface of the iris; *h*, posterior layer of iridal pigment epithelium, partially detached; *i*, *i*, spacia zonularis; *k*, zone of nuclei of the lens fibres; *L*, lens; *l*, ligamentum pectinatum; *M*, longitudinal, and *Mu*, circular fibres of the ciliary muscle; *O*, flattened portion or orbiculus of the ciliary body; *o*, ora serrata; *P*, ciliary processes; *p*, pupillary margin of the iris; *pc*, inner, non-pigmented layer of the ciliary epithelium; *Pe*, retinal pigment epithelium; *pe*, outer or pigmented layer of the ciliary epithelium; *R*, retina; *r*, radial fibres of the ciliary muscle; *S*, sclera; *sc*, canal of Schlemm; *sp*, circular muscle of the iris, the sphincter pupillae; *sl*, suspensory ligament of the lens. $\times 16$. (After Fuchs.)

The meridional fibres form the outer and greater portion of the muscle. They begin just posterior to the corneal margin, taking their origin from the inner surface of the sclera, and radiate backward in a meridional direction for a variable distance, to be finally inserted into the fibrous bundles of the posterior half of the ciliary body, the longest fibre bands passing as far back as the chorio-ciliary junction, where they are attached to the anterior margin of the choroid.

The radial fibres simulate the meridional fibres in that they radiate from the corneal margin. They pursue, however, a shorter course. From their origin they pass backward with a sharp inward curve to assume a direction which approaches that of the radii of the ocular globe (hence their name); they are inserted into the anterior half of the fibrous layer of the ciliary body. Their radial disposition becomes progressively more apparent toward the axial margin of the ciliary body. These fibres are far less numerous than the meridional.

The circular fibres comprise numerous small non-striated muscle bundles which are interspersed among the bundles of radial fibres. They are disposed in a circular direction about the axial margin of the ciliary body on its outer surface, and hence are in relation with the inner surface of the sclero-corneal junction and the outer margin of the base of the iris. The circular muscle fibres are also interspersed among the fibres of the ligamentum pectinatum, which pass in a radial manner from the margin of the posterior homogeneous membrane of the cornea to the base of the iris and anterior margin of the ciliary body. The circular fibres are said to be deficient or even absent in myopic eyes, but are exaggerated in hypermetropic eyes (Iwanoff,* Fuchs†).

The disposition of the ciliary muscle fibres is such that during contraction the fibrous ciliary body and the base of the iris are drawn forward, the choroid is made tense, and the suspensory ligament of the lens is relaxed. The lens then becomes more nearly spherical because of its own elasticity.

The fibrous layer of the ciliary body consists of connective tissue, and connects the fibrous portion of the choroid to the similar tissue of the iris. It is formed by a reticulum of fine fibres in the meshes of which are numerous lamellar and a few pigmented cells. Buried within the outer portion of this fibrous mass and intermingling with its fibres are the fibre bundles of the ciliary

* Stricker's Handbook, vol. iii.

† Textbook of Ophthalmology.

muscle. Into the inner portion of the fibrous layer a vascular plexus is continued from the vascular and capillary layers of the choroid; branches of the ciliary arteries turn forward between the bundles of the ciliary muscle to communicate with this plexus.

Appended to the inner surface of the fibrous layer are numerous meridionally disposed folds of connective tissue which radiate from the base or outer margin of the iris to the margin of the choroid opposite the ora serrata. These are the *ciliary processes*. Their inner or free surface is covered by the pigmented retinal epithelium, and within these processes are contained the greater portion of the pigmented connective tissue cells of the ciliary body. Each fold is much deeper toward its axial margin and becomes progressively diminished in height toward the choroid.

The pigmented epithelial layer is here and there invaginated into the fibrous tissue of the ciliary processes to form ampullate recesses (*the ciliary glands*), which somewhat resemble true secreting glands. These so-called glands have been supposed to be concerned in the secretion of the aqueous humor. They are probably not true secreting glands, but represent mere invaginations of the epithelium.

The ciliary epithelium (*pars ciliaris retinæ, pigment layer of the ciliary body*) consists of a double layer of epithelial cells, continuous posteriorly with the retina, and in front with the pars iridis retinæ. The superficial (innermost) cells present a clear or slightly granular cytoplasm with a centrally situated nucleus. Their cytoplasm is but slightly pigmented, and oftentimes is indistinctly rodlike or fibrillated. In shape, these cells are of the low columnar type, but they become progressively flattened toward the iris, where they are continuous with the pars iridis retinæ.

The cells of the deeper (outer or anterior) layer vary in height from a low columnar at the ora serrata to a somewhat flattened cell near the iridal margin. This cell layer is deeply pigmented, the entire cytoplasm being filled with the dark brown pigment granules. The nucleus, however, as in the pigmented cells of the choroid, contains no pigment, and therefore, in unstained preparations, appears under the microscope as a clear opening in the dark background of pigmented cytoplasm.

THE IRIS (Figs. 417 and 422).—The iris forms an annular curtain which projects from the anterior margin of the ciliary body toward the axis of the eye. It presents a central circular opening, the pupil, which lies in the visual axis.

The iris is suspended in the aqueous humor, its pupillary margin resting gently upon the anterior surface of the lens, its base or ciliary margin being separated from the lens by an interval, the posterior chamber, which is also filled by the aqueous humor.

The iris may be said to consist of *three layers*: 1, the external epithelium; 2, the fibrous stroma; 3, the internal epithelium.

The external epithelium (*endothelium of the iris*) is continuous at the margin of the anterior chamber with the posterior epithelial layer of the cornea, which appears to be reflected upon the anterior surface of the iris. At the pupillary border it is also continuous with the internal epithelium of the iris (*pars iridis retinæ*). The cells of the anterior or external epithelium are very much flattened and almost endothelioid in appearance; at occasional intervals the epithelium is incomplete. These intervals occur either near the pupillary or the ciliary margin, and correspond to recesses which open directly into the fibrous stroma of the iris and become continuous with its lymphatic interstices.

To the naked eye the anterior surface of the iris presents an uneven appearance, which is apparently due to the presence of slight meridional ridges, with shallow intervals, which extend from the pupillary margin of the iris to its outer border.

The fibrous stroma of the iris (*pars choroidalis iridis, pars uvealis iridis*) consists of a loose spongy connective tissue of an almost embryonal type. Its fibres are scanty and are gathered into small bundles, which interlace somewhat, but which are for the most part disposed in a meridional direction. This disposition is especially noticeable near the ciliary margin.

The fibrous stroma is very rich in connective tissue cells, which are mostly stellate and branch and interlace freely. They contain more or less brownish pigment, which is most abundant near the posterior (inner) surface. The color of the iris, when viewed with the naked eye, is dependent upon the depth of pigmentation in these connective tissue cells, as well as in the cells of the internal epithelial layer. In dark blue and black eyes the stroma pigment is scanty, and the very dark epithelial pigment shows through the more anterior layers of the iris. In the brown eye the stroma pigment is dense and opaque. A grey color is produced by a scanty stroma pigment clouded by a rather dense fibrous stroma.

Embedded in the fibrous stroma, near its pupillary margin, is a small bundle of non-striated muscle fibres, which are circularly disposed, to form the so-called *sphincter muscle* of the iris. Its fibres

are distributed in a plane parallel to the surface of the iris, and within the inner (posterior) part of its fibrous stroma. They are most abundant near the pupillary margin, and become progressively thinner toward the base of the iris. Internally to the sphincter muscle, and in contact with the basement membrane of the internal epithelium, is an incomplete layer, more distinct toward the ciliary margin of the iris, which contains radially disposed smooth muscle fibres, the *dilator muscle* of the iris.

The stroma of the iris is exceedingly vascular, the arteries and veins being meridionally disposed, the capillaries forming an irregular plexus. Near the pupillary margin the vessels form a rich capillary anastomosis, the *circulus minor*. The entering arteries likewise form a *circulus major* by anastomoses at the ciliary margin of the iris.

The internal epithelium (*posterior epithelium, pigment epithelium of the iris, pars iridis retinæ*) resembles that of the ciliary body or *pars ciliaris retinæ*, with which it is continuous. The innermost (superficial) layer of epithelial cells, in the iridal epithelium, is deeply pigmented and somewhat flatter than in the ciliary body. The pigmentation is so deep that in the adult iris it is scarcely possible to distinguish the two epithelial layers. These can, however, be readily seen in the fetal eye, and even in that of the child. In albinos the pigment of the epithelium, as well as that of the stroma, is very scanty, or may even be entirely absent.

THE ANTERIOR CHAMBER is bounded in front by the posterior (internal) surface of the cornea, and behind by the anterior surface of the crystalline lens and the anterior (external) aspect of the iris; it contains the aqueous humor. Its anterior boundary is convex, its posterior concave, and its circular margin is limited by an area which is known as the *irido-corneal angle*.

At this angle the epithelium is reflected from the posterior surface of the cornea upon the anterior surface of the iris. The latter portion of the epithelial layer is incomplete, since it presents numerous openings which communicate with the lymphatic spaces between the fibres of the ligamentum pectinatum and ciliary muscle. These lymphatic recesses are the *spaces of Fontana*.

The ligamentum pectinatum consists of fibres which arise from the margin of Descemet's membrane, and pass backward and inward, in a radial direction, to the fibrous stroma of the iris and ciliary body. Viewed from the cavity of the anterior chamber the fibres of this ligament, with the intervening spaces of Fontana,

present a toothed appearance ; the ligament derives its name from this peculiarity.

THE POSTERIOR CHAMBER is an annular cavity, somewhat triangular or trapezoidal in transection, whose lumen, like that of the anterior chamber, is occupied by aqueous humor, suspended in which are the fibres of the suspensory ligament of the crystalline lens.

It is limited anteriorly by the internal surface of the iris, and antero-externally by the ciliary processes. Its postero-internal boundary is formed by the marginal portion of the lens, together with the adjacent portion of the hyaloid membrane, which incloses the vitreous humor.

THE INTERNAL COAT

The internal coat of the eyeball is divisible into three portions : 1, the *pars optica retinæ* or *retina* proper ; 2, the *pars ciliaris retinæ*, and 3, the *pars iridis retinæ*.

The last two portions, though morphologically continuous with the *pars optica retinæ*, differ therefrom in their physiological function ; they respectively form the innermost layer of the ciliary body and iris. As such they have already been described.

The Retina.—The retina (*pars optica retinæ*) may be said to be formed by the radial expansion of the fibres of the optic nerve which enters the eye at the inner side of its posterior pole, piercing the sclera and choroid and spreading out over the inner surface of the eyeball.

These nerve fibres arise from groups of nerve cells which are disposed in layers to form the optic and retinal ganglia (*ganglion nervi optici* and *ganglion retinæ*). The association of nerve cells and fibres with their supporting tissues forms the inner, *cerebral*, or *neural portion* of the retina. The dendritic arborizations of many of these nerve cells lie within the outer half, or *neuro-epithelial portion* of the retina.

The retina may be said to extend forward from the entrance of the optic nerve as far as the posterior margin of the ciliary body, where it apparently ends abruptly with an indented border, the *ora serrata*. From this border the retina is continued farther forward, but only as the dark pigmented layers of the ciliary processes and iris. In the usual preparations these layers contrast intensely with the opaque white color of the true retina. Like all the other tissues which are placed in the optical axis of the eye, the retina, during

life, with the exception of its pigment layer, is perfectly transparent, but becomes opaque immediately after death or local injury.

The retina presents on its inner surface a slightly elevated yellow spot, the *macula lutea* (*limbus lutea*), which lies exactly at the posterior pole of the visual axis. The *fovea centralis* is the slight depression in the center of the macula lutea, and is the result of an apparent thinning of the retinal layers at this point.

The papilla optica, or entrance of the optic nerve, also forming a slight elevation with a central depression, is placed 0.5 to 1 mm. to the inner side of the macula lutea, and at a slightly lower horizontal plane.

Development.—A word as to the development of the organ will make clearer the description of the several layers of the retina. The

retina is developed as an evagination of the first cerebral vesicle, and is, therefore, to be regarded as a detached lobe of the

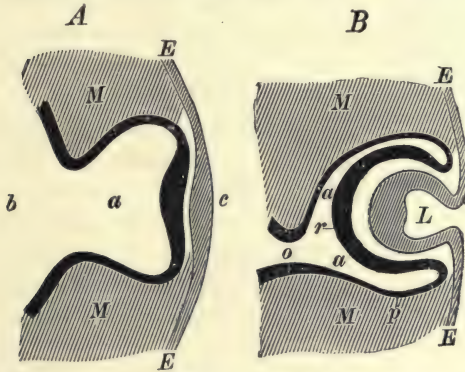


FIG. 423.—THE DEVELOPING EYE IN TRANSECTION; DIAGRAMMATIC.

A, early; B, later stage. E, E, ectoderm; L, lens; M, M, mesoblast; a, optic vesicle, protruding from, b, the first cerebral vesicle; c, a thickening of the ectoderm, anlage of the lens; o, constricted pedicle of the optic cup; p, outer coat of the optic vesicle, anlage of the retinal epithelium; r, inner wall of the vesicle, anlage of the neural portion of the retina. (After Fuchs.)

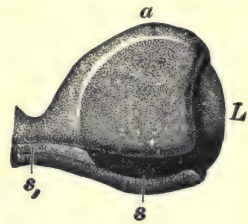


FIG. 424.—SCHEMATIC RECONSTRUCTION OF THE DEVELOPING EYE.

a, optic cup; s, fissure; s1, optic nerve; L, developing lens. (After Fuchs.)

cerebrum itself. The evagination grows forward in the embryo, and soon forms a flask-shaped process whose expanded extremity is early infolded in a cup-like manner. The inferior surface of this optic cup at first presents a slit-like deficiency, into which grows the mesoblastic tissue which ultimately forms the vitreous humor and conveys the central artery of the optic nerve. The indented extremity of the optic cup is soon occupied by the developing lens, which arises, under the influence of the optic cup

itself (Lewis*), but is formed from the overlying area of the ectoderm.

THE LAYERS OF THE RETINA.—The retina may be said to consist of ten layers, which from without inward are :



FIG. 425.—THE RETINA OF A CHILD'S EYE; MERIDIONAL SECTION.

a, nerve fibre layer, the broad bases of Müller's fibre cells show distinctly; *b*, blood vessel; *c*, large ganglion cell layer; *d*, inner reticular layer; *e*, inner nuclear layer; *f*, outer reticular layer, with a prominent fibre layer of Henle; *g*, outer nuclear layer; *i*, layer of pigmented epithelium; *k*, choroid coat. Hematein and eosin. Photo. $\times 225$.

1. The pigment epithelium.
2. The layer of rods and cones.
3. The external limiting membrane.
4. The outer nuclear layer.
5. The fibre layer of Henle.
6. The outer reticular layer.
7. The inner nuclear layer.
8. The inner reticular layer.
9. The ganglion cell layer.
10. The nerve fibre layer.

To these several layers an additional one, the internal limiting membrane, is frequently added. The first five of these layers are contained within the neuro-epithelial portion of the retina, the last five form its cerebral or neural portion.

1. **The pigment epithelium** (*layer of pigment cells*) consists of a single layer of columnar epithelial cells whose bases rest upon and are firmly adherent to the inner surface of the choroid coat, and from whose free borders irregular processes extend inward between the elements of the rod and cone layer. These epithelial cells have a finely granular cytoplasm. Their nucleus is oval, somewhat flattened, and placed near the base of the cell; it is, however, obscured or even entirely hidden by the mass of dark pigment granules by which the cytoplasm of the cell is more or less completely filled.

The disposition of the pigment within the epithelial cell apparently corresponds to, and is dependent upon, the effect of light upon the retina. In an eye exposed to the action of light at the

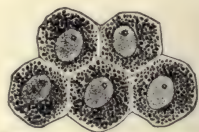


FIG. 426.—PIGMENTED EPITHELIUM OF THE RETINA VIEWED IN TRANSECTION.

$\times 500$. (After Fuchs.)

instant of death, the pigment granules accumulate in the irregular processes of the cells which surround the rods and cones, the outer or basal portion of the cell being relatively free from pigment. In an eye which is shaded from the light, or in one removed in comparative darkness, the pigment has apparently retracted until it lies entirely within the body of the cell. Even under these conditions the extreme base of the cell frequently presents a narrow zone which is relatively free from pigment. Similar changes in the disposition of the pigment undoubtedly occur in the living eye under the influence of exposure to varying degrees of light.

The function of this pigment and of the peculiar changes in its disposition is still somewhat speculative, but it may, without doubt, be safely asserted that these phenomena are concerned with the renewal of the visual purple of the rods and cones after the same has been bleached by exposure to light. Possibly these changes possess a stimulant action upon the neuro-epithelial elements.

2. The rod and cone layer (*bacillary layer*) consists of a series of columnar elements which are disposed in a palisade-like manner, and whose narrow extremities are embedded in the surface of the layer of pigment epithelium. The rod and cone layer contains elements of two distinct types, the rods and the cones, which are nevertheless very similar to each other in their structure. Each rod and each cone consists of two distinct portions, the outer of which, alone, lies in the bacillary layer; the inner segment is included in the outer nuclear layer of the retina. The outer segment is cytoplasmic, and its broad base rests upon the external limiting membrane; the inner portion is narrow, nucleated near its center, and extends entirely through the outer nuclear layer.

The Rods.—The outer, cytoplasmic, or bacillary portion of each rod consists of a somewhat thickened base and an outer filamentous extremity. These two portions are quite as distinct in fresh unstained tissue as in fixed and stained preparations, the distinction being due to the fact that the inner segment of each rod, while finely granular and easily stained, is also singly refractive; the outer segment, on the other hand, not only stains with difficulty but is doubly refractive. The outer, therefore, under all conditions appears bright and lustrous as compared with the isotropic inner portion.

The outer segment contains the *visual purple* or *rhodopsin* which, during life, is rapidly bleached by exposure to light, and is as rapidly renewed through the agency of the pigment epithelium.

Both segments, but especially the inner, under favorable conditions present slight longitudinal striations. These striations, when present, are most distinct in the outer half of the inner rod

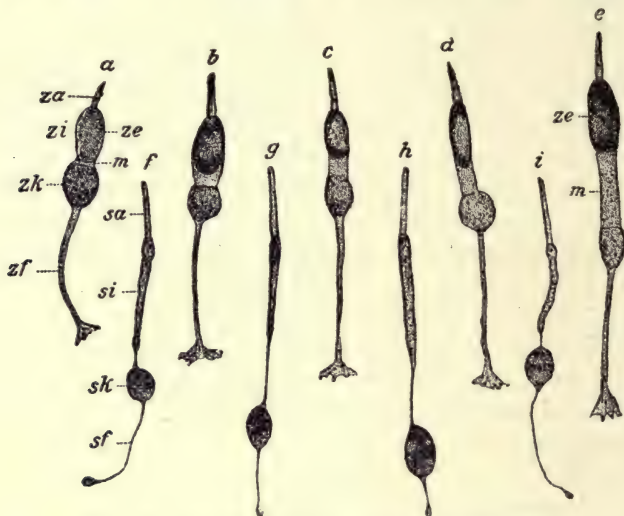


FIG. 427.—ISOLATED ROD AND CONE CELLS OF THE PIG.

a-e, cones; *f-i*, rods; *za*, outer portion, *zi*, inner portion of the cone, the latter consisting of an ellipsoid part, *ze*, and a more or less elongated neck part, *m*; *zk*, cone nucleus; *zf*, cone fibre; *sa*, outer, and *si*, inner portion of the rod; *sk*, rod nucleus; *sf*, rod fibre. (After K  lliker.)

segment. The outer filamentous portion of each rod sometimes exhibits transverse markings, possibly indicating a minute structure which is comparable to a series of superposed disks.

The inner or nucleated portion of each rod, the *rod fibre*, is found in the outer nuclear layer and is continued as a fine filament, which, having penetrated the external limiting membrane, extends as far as the border line between the outer nuclear and outer reticular layers, at which level the rod filament ends in a knob-like expansion. At some point in its course through the nuclear layer the rod fibre presents a nucleated enlargement, which, under some conditions, shows one or two alternate light and dark transverse striations. The nuclei of the rod fibres are placed at various levels in the nuclear layer, and collectively occupy nearly its entire thickness. Its outer border, however, contains relatively few rod nuclei.

The cones resemble the rods in structure, but their cytoplasmic segment is shorter and several times as broad. The outer aniso-

tropic portion is especially short, while the isotropic basal portion, whose longitudinal striations occupy a somewhat greater proportion of its length than is the case with the rod segment, rests directly upon, and may even project through the external limiting membrane. The inner or nucleated portion, therefore, begins as a broad nucleated mass, equal in diameter and continuous with the bacillary portion of the cone element, to which it is oftentimes united by a slightly constricted neck. In this inner segment, just within the external limiting membrane, is the cone nucleus; it differs from the rod nucleus in that it stains less deeply, presents no trans-

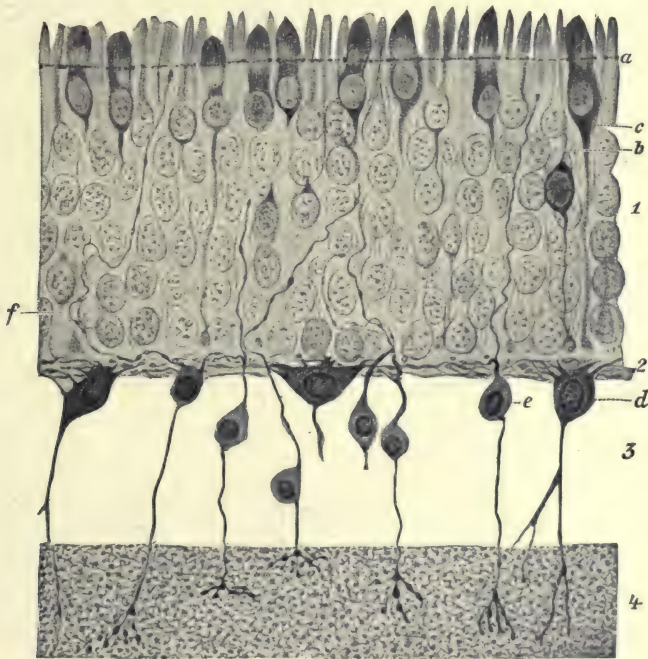


FIG. 428.—FROM THE HUMAN RETINA.

1, outer nuclear layer; 2, outer reticular layer; 3, inner nuclear layer; 4, inner reticular layer; a, external limiting membrane; b, rod nuclei; c, cone nuclei; d, cone bipolars; e, rod bipolars; f, an exceptionally long process of a rod bipolar. Methylen blue. Highly magnified. (After Dogiel.)

verse striations, and frequently incloses a distinct nucleolus. From its nucleated portion the *cone fibre* is continued as a rather broad cytoplasmic filament straight inward to the border of the nuclear layer, where it terminates in an expanded portion or *cone foot*,

from the flattened inner surface of which fine filaments penetrate the margin of the outer reticular layer.

The outer segments of both rods and cones are embedded in the cells of the pigment layer, whose delicate filamentous processes project between the rods and cones, frequently extending almost

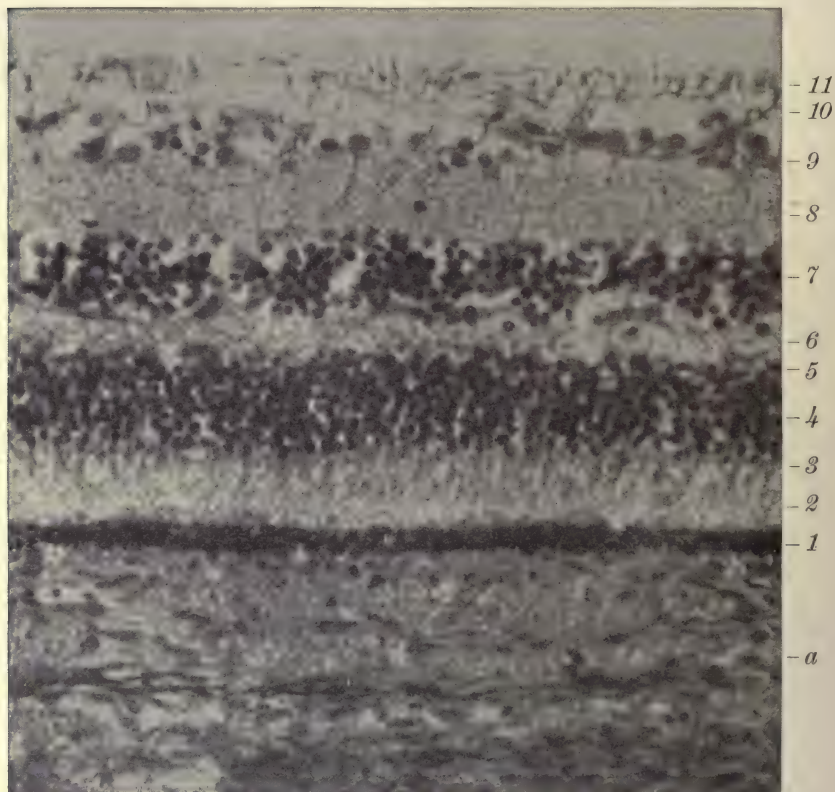


FIG. 429.—FROM A MERIDIONAL SECTION OF A CHILD'S EYE, SHOWING THE LAYERS OF THE RETINA AT A POINT NEAR THE MARGIN OF THE MACULA LUTEA.

1, pigment layer; 2, bacillary layer; 3, external limiting membrane (indistinct); 4, outer nuclear layer; 5, fibre layer of Henle; 6, outer reticular layer; 7, inner nuclear layer; 8, inner reticular layer; 9, ganglion cell layer; 10, nerve fibre layer; 11, internal limiting membrane (more distinct in Fig. 430); a, choroid coat. Hematein and eosin. Photo. $\times 400$.

to the external limiting membrane. Both rods and cones are hexagonal or nearly circular in transection. The slight intervals between the neighboring elements and the processes of the pigment

epithelium are occupied by a homogeneous fluid, probably a somewhat modified lymph.

3. The **external limiting membrane** (*membrana limitans externa*) consists of the flattened and amalgamated extremities of

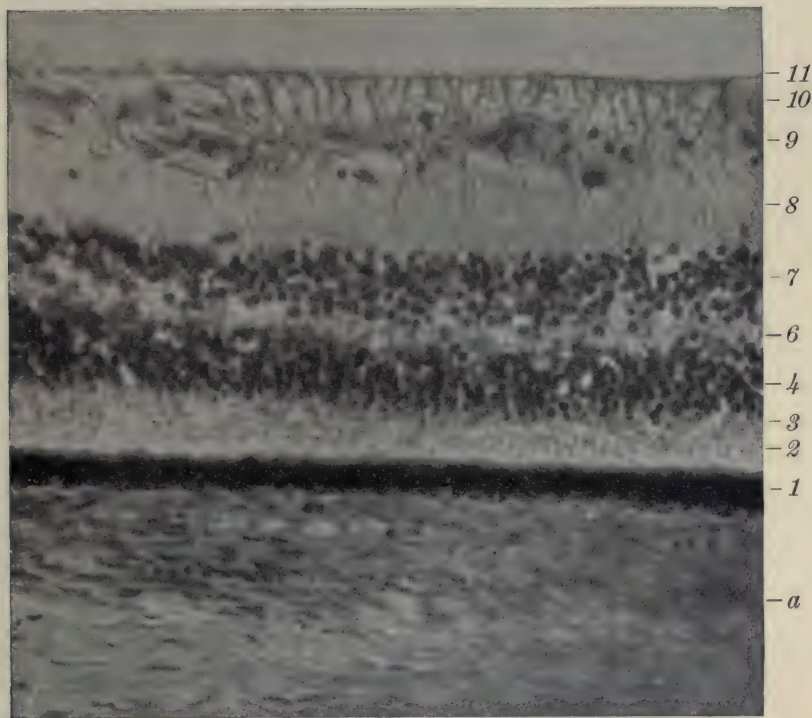


FIG. 430.—FROM A MERIDIONAL SECTION OF A CHILD'S EYE, SHOWING THE LAYERS OF THE RETINA AT A POINT MIDWAY BETWEEN THE MACULA LUTEA AND THE ORA SERRATA.

References as in Fig. 429. Hematein and eosin. Photo. $\times 400$.

Müller's fibres, which form the chief supporting tissue, the neuroglia element, of the retina, and which extend from the extreme inner surface outward to the external limiting membrane. It will therefore be more convenient to defer further description of this membrane until the remaining layers have been described, and the Müllerian fibres can be considered in their entirety.

4. The **outer nuclear layer** (*outer granular layer*) consists, for the most part, of the nucleated portions of the rod and cone elements. The outermost zone of this layer contains only cone nuclei; the inner portion, comprising about three-fourths of its

thickness, contains only rod nuclei. The former, with occasional exceptions (Stöhr *), are situated in only one relatively narrow plane; the latter are distributed at various levels, though they occur more abundantly in the mid-region of the nuclear layer. In addition to portions of Müller's fibres which serve for the support of the nucleated elements, this layer contains the terminal filaments of the distal processes of some of the small bipolar nerve cells of the inner nuclear layer.

5. **The fibre layer of Henle** is formed by that portion of the cone fibres which is internal to the layer of rod nuclei. It is a thin layer and only acquires importance in the neighborhood of the macula lutea, where the cones are most abundant. In this portion of the retina it is easily distinguished from the outer reticular layer by the somewhat radial disposition of its fibres, the fibres of the reticular layer having an irregularly meridional direction.

6. **The outer reticular layer** (*outer molecular layer*) presents a dense tangle of neural tissues consisting of supporting neuroglia fibres and interlacing processes from the horizontal and bipolar nerve cells of the inner nuclear layer. Terminal fibrils from this network intermingle in the fibre layer of Henle with terminal fibrils from the cone feet; more externally they are in intimate relation with the end knobs of the rod fibres. This arrangement permits the transmission of stimuli from the neuro-epithelium to the retinal ganglion.

7. **The inner nuclear layer** (*inner granular layer, ganglion retinae, outer ganglionic layer*) contains a mass of nerve cells, together with the nucleated portion of the fibre cells of Müller. The nerve cells may be described as corresponding to one of *three types*, which, from the plane in which they are distributed may be termed the outer, middle, and inner.

The outer nerve cells (*horizontal cells, basal cells*) possess pyramidal, stellate, or flattened cell bodies whose dendrites are distributed to the horizontal plexus of the outer reticular layer. These cells vary in size; the dendritic or distal processes of the larger cells on reaching Henle's layer are in relation with the terminal fibrils of the cone feet; those from the smaller nerve cells are in relation with the terminal knobs of the rod fibres. The axis cylinders or central processes from all these cells after traveling horizontally—viz., in a plane parallel to the layers of the retina—for a greater or less distance, turn inward and pass to the inner reticular

* Verhandl. d. phys. med. Gesellsch., Würzburg, 1887.

layer, where they come into relation with the dendrites of the large nerve cells of the ganglion cell layer. Other processes, mostly from the smaller cells, terminate in the outer reticular layer, probably serving the purpose of association neurones.

The nerve cells of the **middle type** are usually of bipolar form, and are the most abundant elements of the outer nuclear layer.



FIG. 431.—HORIZONTAL CELL FROM THE RETINA OF A CALF.

a, cell body; b, neuraxis; c, terminal arborizations of the neuraxis. Golgi's stain.
× 150. (After Marenghi.)

The one set of their processes is directed outward (peripheralward); they pass to the outer reticular layer where they eventually come into relation with either the rod fibres or the cone fibres. Hence those cells which are in relation with the visual rods are classified as *rod bipolars*, those in relation with the visual cones as *cone bipolars* (Fig. 428). The terminal fibrils of the cone bipolars are horizontally, those of the rod bipolars radially disposed.

The central processes, neuraxes, of the bipolar cells are directed inward (centralward), and on entering the inner reticular layer terminate in an end brush which is in relation with the dendritic processes from the large ganglion cell layer.

The **inner nerve cell type** (*amacrine cells of Cajal, spongioblasts of Kölliker*) are large nerve cells which occupy a nar-

row zone at the inner margin of this nuclear layer. These are large stellate cells whose dendritic processes extend into the inner reticular layer and take part in the formation of the dense felt-work of which that layer consists. The course of the axis cylinders of these cells is still a matter of some doubt. Ramón y Cajal, believing these cells to possess no neuraxis, designated them "amacrine cells" and subdivided them according as their dendrites were



FIG. 432.—TWO AMACRINE CELLS OR SPONGIOLASTS FROM A TRANSECTION OF THE RETINA OF A CALF.

Golgi's stain. $\times 260$. (After K  lliker.)

distributed in either one of several horizontal planes (the number varying in different species) or diffusely throughout the inner reticular layer.

Some of the amacrine cells, however, send a neuraxis in a horizontal direction to the inner reticular layer, and are also in relation with the terminal arborizations of centrifugal nerve fibres which enter from the nerve fibre layer. These have been regarded by some observers as "dislocated nerve cells" of the ganglion cell layer; Cajal named them "*association amacrines*."

8. **The inner reticular layer** (*inner molecular layer, inner plexiform layer, neurospongium*) is a densely tangled network of nerve-cell processes, a neurospongium. To these are added a much branched portion of M  ller's fibres, which form the chief supporting tissue of this layer. The cell processes entering into this formation are derived from the cells of the inner nuclear and ganglion cell layers, and it is here that the processes of these cells interlace so closely as to permit the transmission of impulses from the one neurone to the other. Their terminal arborizations are, for the most part, disposed in horizontal planes, though a few spread throughout the entire thickness of the reticular layer.

9. **The ganglion cell layer** (*ganglion nervi optici, inner ganglionic layer, layer of large nerve cells*) is of variable thickness. Its greatest depth is in the region of the macula lutea, where it consists of five or six superposed ganglion cells. Toward the equator of the eye it becomes progressively thinner, until near the ora serrata its single layer of cells only forms an incomplete stratum.

The cells comprising this layer are mostly large, stellate, pyriform, or spheroidal nerve cells, from whose peripheral border dendrites pass to the inner reticular layer, and from whose central border a neuraxis passes to the nerve fibre layer to eventually become the neuraxis of a fibre of the optic nerve.

These cells, though varying much in size and shape, are mostly composed of a clear cytoplasm and possess a distinct nucleolus. Intermingled with the nerve cells are many branches of the Müllerian fibres which here form an open meshed network within whose spaces the nerve cells are inclosed.

10. **The nerve fibre layer**, in intimate relation with the preceding, forms the innermost of the retinal zones. It consists of naked axis cylinders passing from their origin in the ganglionic layers to their immediate destination, the optic nerve. They are, therefore, mostly if not wholly centripetal fibres. A few centrifugal fibres have been demonstrated in this layer, but they would appear to be probably vaso-motor in function.

The nerve fibres of this layer converge from all portions of the retina, follow a meridional course through the open meshes of the network of branching Müllerian fibres, and converge toward the optic papilla, the entrance, or rather the point of exit, of the optic nerve. Hence the nerve fibre layer, being augmented by the constant acquisition of new neuraxes from the ganglion cells, becomes progressively thicker toward the posterior pole of the eye, and is thickest at the margin of the optic papilla, where it is so highly developed as to almost exclude the other retinal layers.

The course of these non-medullated nerve fibres is not straight; on the contrary, they interlace to form a delicate fibrillar network. At the margin of the papilla optica the nerve fibres bend outward



FIG. 433.—A NERVE CELL OF THE LARGE GANGLION CELL LAYER; FROM THE RETINA OF A CAT.

n, n, neuraxis; *c, c*, collaterals. Golgi's stain. $\times 325$. (After Kölliker.)

with a sharp curve almost at right angles to their former course. At this point also they gradually acquire a medullary sheath, and, uniting into many bundles, penetrate the numerous openings of the laminae cribrosae of the sclerotic and choroid coats to form the optic nerve.

THE SUPPORTING TISSUES OF THE RETINA.—These consist of a gliaform reticulum distributed throughout the cerebral portion of the retina, and of a special supporting tissue, Müller's fibres, which may also be regarded as glia tissue, though they are common to both the neural and epithelial portions.

The fibres of Müller comprise numerous large glia cells whose processes begin with an expanded base at the inner surface of the nerve fibre layer, and can be traced all the way through the retina to the membrana limitans externa, which is likewise formed by the terminal expansions of these cells. The nucleus of the fibre cell lies in the mid-region of the inner nuclear layer.

The expanded and flattened bases or inner extremities of these glia cells are so closely approximated to one another as to form a complete investment for the inner surface of the retina, which is known as the *internal limiting membrane* (*membrana limitans interna*) and is frequently classed as the innermost layer of the retina. Under low magnification it appears as a continuous membrane, but under higher powers it is readily resolved into the broad, conical, basal expansions of which it consists. From these initial expansions the glia cells may be traced outward through the



FIG. 434.—A FIBRE CELL OF MÜLLER FROM THE DOG'S RETINA.

1, nerve fibre layer; 2, ganglion cell layer; 3, inner reticular layer; 4, inner nuclear layer; 5, outer reticular layer; 6, outer nuclear layer; a, a process extending into the inner reticular layer; b, nucleus of the cell; m. l. e., external limiting membrane; m. l. i., internal limiting membrane. Golgi's stain. Highly magnified. (After Cajal.)

nerve fibre and ganglion cell layers by means of the numerous coarse processes or glia fibres.

The glia fibres then pass in a fairly straight course through the inner reticular layer. In this portion numerous short, fine, lateral offshoots from the main stem support the neurospongium of the reticular layer. Continuing through the inner nuclear layer the glia substance is somewhat thickened; it sends off fewer but coarser lateral processes, and in the mid-region of this layer presents an enlargement which is almost entirely occupied by the large ovoid nucleus.

The fibre cell, somewhat narrowed, may then be traced through the outer reticular to the outer nuclear layer, where its processes form a dense network about the nucleated segments of the rod and cone elements.

The terminal processes of the fibre cells become again flattened, somewhat after the manner in which the internal limiting membrane is formed, and are so closely approximated as to form an *external limiting membrane*, a distinctly membranous structure which derives a reticular appearance from being pierced by each of the innumerable rod and cone elements.

From the outer surface of the expanded ends of the Müllerian fibre cells which form the external limiting membrane, minute fibrils are continued between the bases of the non-nucleated portions of the rod and cone cells to form shallow sockets, the *rod and cone sockets*, into which the bacillary portions of these elements are fixed.

THE MACULA LUTEA (*limbus lutea*, *yellow spot*), being apparently the most highly developed portion of the retina, deserves some special consideration. The macula is a circular elevation in the center of which is a marked depression, the *fovea centralis*. The elevation results from an increased thickness of all the retinal layers, but especially of the ganglion cell layer, which in this portion of the retina is five or six cells deep. The reticular layers are also much thickened in this area. In the bacillary layer, within the area of the macula, the cones are far more numerous than elsewhere, especially when considered in relation to the rods, which are greatly diminished.

Toward the *fovea centralis* the inner layers of the retina become very much thinned, until at its center the nerve tissues are merely represented by scattered cells of the inner nuclear and ganglion cell layers. Rod elements are not found in this area; the bacillary layer consists entirely of cones. The much elongated nuclear portion of the cones deviates in a slanting direction toward the margin of the macula, and the cone nuclei are further removed from the external

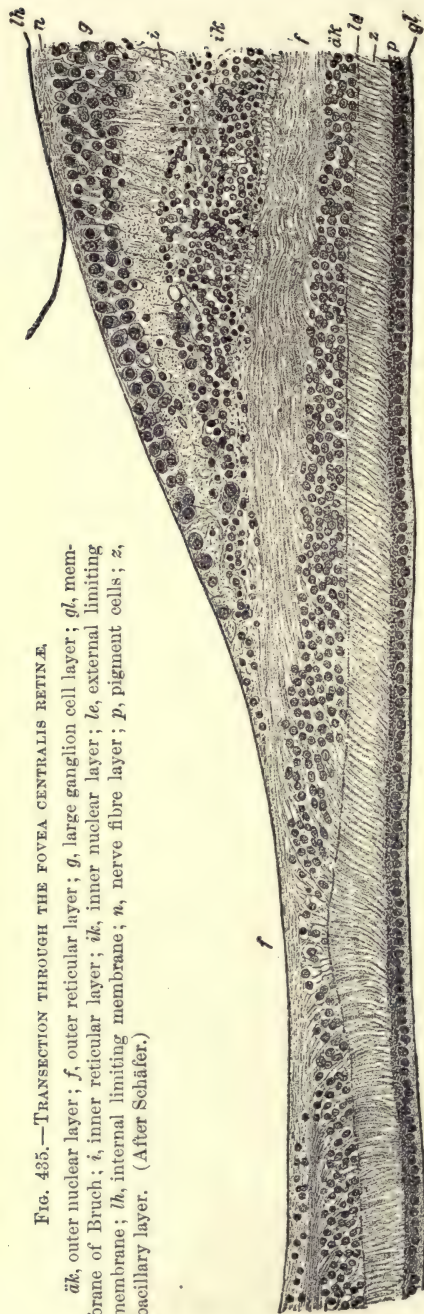


FIG. 435.—TRANSECTION THROUGH THE FOVEA CENTRALIS RETINÆ.

gl, outer nuclear layer; *g*, outer reticular layer; *g*, large ganglion cell layer; *gl*, membrane of Bruch; *i*, inner reticular layer; *ik*, inner nuclear layer; *le*, external limiting membrane; *lh*, internal limiting membrane; *n*, nerve fibre layer; *p*, pigment cells; *z*, bacillary layer. (After Schäfer.)

limiting membrane than elsewhere in the retina.

The pigment of the epithelial layer is much diminished and may even be absent at the fovea. Because of the diminution in the number of ganglion cells in this area the nerve fibre layer is greatly diminished in thickness on approaching the margin of the fovea, and toward its center entirely disappears.

THE OPTIC NERVE is a large nerve trunk, composed, like the white matter of the brain of which it is an ontogenetic portion, of medullated nerve fibres without a neurilemma. It receives an investing sheath from each of the cerebral membranes. These sheaths are continued as far forward as the eyeball, at which point they become continuous with the sclera.

Lying in the axis of the nerve, the arteria centralis retinæ with its accompanying vein enters the eye and appears on the inner surface of the retina at the *porus opticus* in the center of the *optic papilla*. Here it divides, its several branches at first pursuing a meridional course between the hyaline membrane and the retinal surface; soon they pierce the latter to supply the cerebral portion of the retina. No vessels penetrate

the neuro-epithelial portion of the retinal layers. The vena centralis retinae pursues a course exactly similar to that of the artery.

The Ora Serrata (Fig. 417).—At the ora serrata the typical layers of the retina, already much thinned, abruptly cease. They are continued forward only as the double layer of epithelial cells belonging to the pars ciliaris retinae, the inner stratum of which appears to be analogous to and continuous with the cerebral portion of the retina, while the outer, deeply pigmented layer apparently represents the outer or neuro-epithelial portion of the retinal tissues.

THE OCULAR CONTENTS

Within the ocular globe, whose walls are formed by the three coats of the eye, are certain structures which may be collectively considered as its contents. They are:

1. The aqueous humor.
2. The crystalline lens.
3. The vitreous humor.
4. The hyaloid membrane.
5. The suspensory ligament.

THE AQUEOUS HUMOR.

—The aqueous humor is a fluid, closely allied to lymph, which occupies the anterior and posterior chambers of the eye. Microscopically it is structureless.

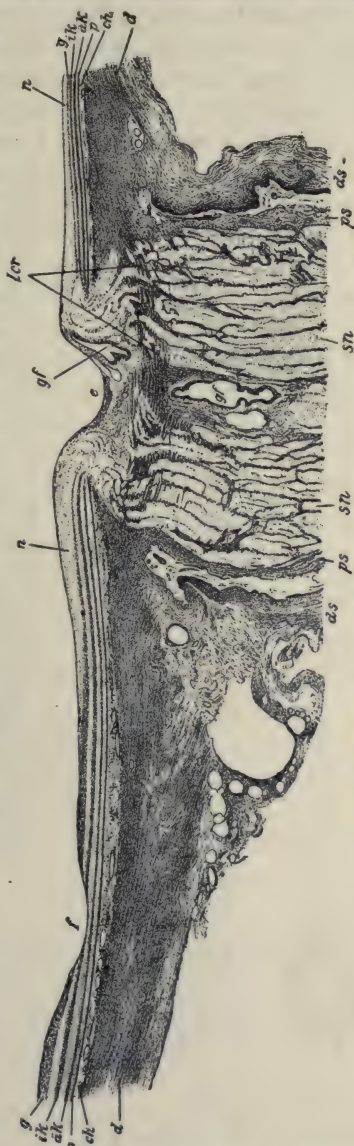


FIG. 436.—ENTRANCE OF THE OPTIC NERVE.

ak, outer granular layer of the retina; *dk*, choroid coat; *ds*, dural sheath; *e*, depressed center of the optic papilla; *f*, fovea centralis; *gf*, layer of ganglion cells; *gf*, blood vessels; *dk*, inner granular layer; *ler*, lamina eribrosa; *n*, nerve fibre layer; *p*, pigment layer; *ps*, pial sheath; *sn*, funiculi of optic nerve fibres. × 17. (After Kölliker.)

THE CRYSTALLINE LENS.—The crystalline lens with its suspensory ligament forms a sort of diaphragm which separates the ocular cavity into two compartments, of which the anterior is occupied by the aqueous humor, the posterior by the vitreous humor.

The lens is a biconvex transparent body having a somewhat greater convexity on its posterior than on its anterior surface; its curvature is greater at its margin than toward its center. It consists of a capsule, epithelium, and a substantia lentis.

The capsule of the lens is a homogeneous membrane which covers its entire surface and receives the attachment of the suspensory ligament. It presents faint meridional striations and may sometimes be separated into several lamellæ (Berger*); this lamellation may be purely artificial, but appears to be somewhat dependent upon the attachment of the fibres of the suspensory ligament to the surface of the lenticular capsule.

The capsule is about twice as thick over the anterior as over the posterior surface of the lens. On the former surface it is in relation with the lenticular epithelium, but on the posterior surface the capsule rests directly upon the substantia lentis. The anterior

surface of the capsule is in gentle contact with the free margin of the iris.

The lenticular epithelium consists of a single layer of cells which covers the entire anterior convexity of the lens, extending as far back as its equator. The height of these cells varies with the age of the individual. In fetal life they are distinctly columnar, in youth short columnar or cuboidal, in adult life low cuboidal or flattened. Toward the margin of the lens the epithelial cells become progressively elongated, and at its equator are transformed directly into the fibres of the lenticular substance.

The substantia lentis is, therefore, the product of the epithelium of the lens, whose cells become greatly elongated to form slender hexagonal prisms, known as the lens fibres.

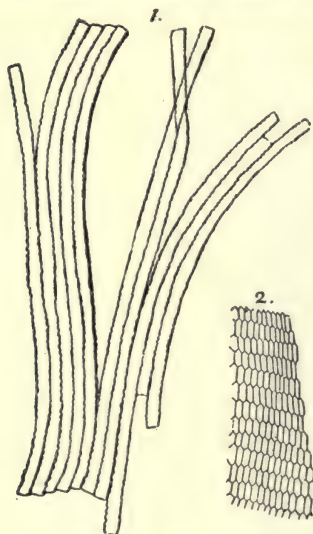


FIG. 437.—LENS FIBRES.

1, in profile, from the crystalline lens of the ox's eye; 2, in transection, from the human crystalline lens. $\times 350$. (After Kölliker.)

* Anat. norm. et path. de l'œil, 1893.

When it is first formed each prism exhibits a nucleus which persists for some time, but gradually disappears as in the process of growth the older fibres become farther and farther removed from their source of nutrition, the lymph and the aqueous humor in which the surface of the lens is bathed. This change is accompanied by a hardening or cornification and slight shrinkage

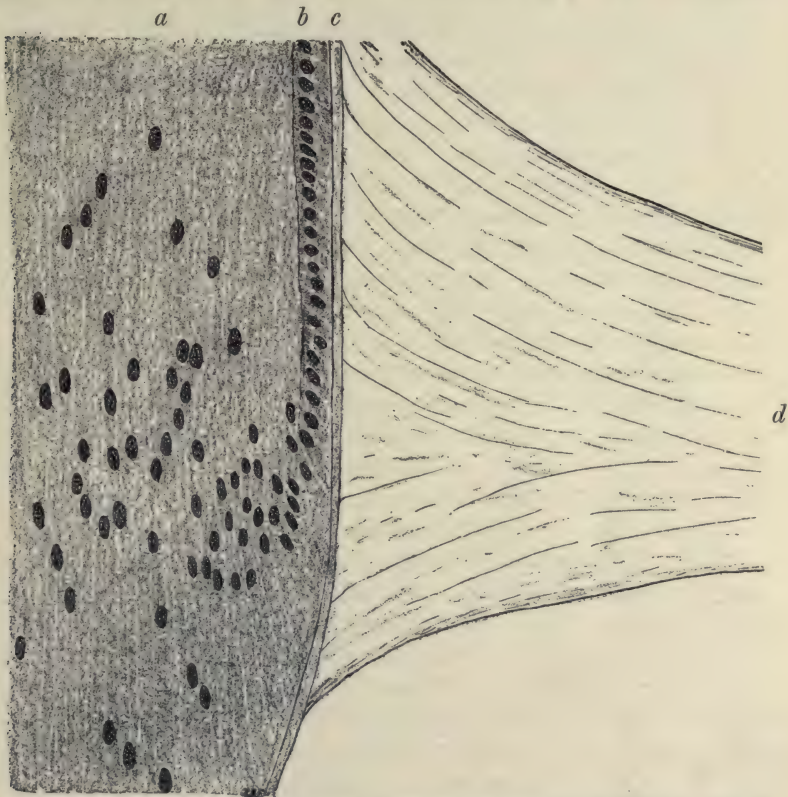


FIG. 438.—THE NUCLEAR ZONE AT THE MARGIN OF THE CRYSTALLINE LENS OF A CHILD'S EYE, SHOWING THE TRANSITION OF THE LENS EPITHELIUM TO THE LENS FIBRES AND THE ATTACHMENT OF THE SUSPENSORY LIGAMENT.

a, lens fibres; *b*, lenticular epithelium; *c*, capsule of the lens; *d*, suspensory ligament. Hematein and eosin. $\times 273$.

of the lens fibres, so that those prisms which come to occupy the center of the lens form a dense, hard mass of non-nucleated fibrous cells with faintly serrated margins; the peripheral fibres retain their smooth edges and their nuclei, and form a protoplasmic mass

of much softer consistency. The hardened central mass is the so-called *nucleus of the lens*.

The nuclei of the lens fibres remain in the neighborhood of the equator, where they are first formed, and are thus contained within a narrow, superficial, equatorial zone, the *nuclear zone*.

Each lens fibre is disposed along a meridian of the lens, and extends from its anterior to its posterior hemisphere; the fibres are so arranged that they abut upon one another, end to end, along Y-shaped lines which radiate from either pole. This union is often quite firm, and thus are formed long fibrous bands which can be traced from the anterior to the posterior hemispheres of the lens. These bands are distributed in a peculiar manner. Near each pole along the line of abutment, the band may be said to bend upon itself with a sharp curve—making an angle of about 60° —whose convexity is directed toward the pole, the parallel fibres being so arranged as to form a sector whose apex is also directed toward the pole. The corresponding sectors of opposite poles overlap one another so that the fibrous bands are continued from one side of one polar mass to the reverse side of the overlapping sector and so back, on the farther side, to the adjacent sector of the former hemisphere. By teasing, fibrous bands can sometimes be traced successively through all of the polar sectors and thus back to a sector beneath that from which the start was made. Obviously no individual lens fibre is of sufficient length to extend from pole to pole of the lens.

THE VITREOUS HUMOR.—The vitreous humor (*vitreous body*) is a soft jelly-like mass which fills the entire cavity of the eye behind the line of the ora serrata and crystalline lens. It is completely invested by the hyaloid membrane. The vitreous humor appears to be a peculiarly delicate form of very loose gelatinous connective tissue whose scanty fibres present a somewhat concentrically lamellated arrangement and are so very delicate as to be recognized under ordinary conditions only with the greatest difficulty.

Occasionally stellate and fusiform cells, remarkable for their large vacuoles and varicose processes, have been demonstrated in small numbers within the vitreous body. Small rounded cells somewhat resembling leucocytes are also found, but for the most part they are flattened against the hyaloid membrane; they occur in very limited numbers.

THE HYALOID MEMBRANE.—The hyaloid membrane is a very thin structure which surrounds the vitreous humor and unites it to the inner surface of the retina and the crystalline lens. It

consists of delicate glassy fibres so disposed as to form an extremely thin reticular membrane.

This membrane passes forward over the inner surface of the retina, to which it is loosely united, until at the ora serrata its fibres leave the retinal surface and pass inward to the margin of the lens to become firmly adherent to the posterior surface of the lenticular capsule.

THE SUSPENSORY LIGAMENT.—Certain fibres from the hyaloid membrane pass forward from the ora serrata and are firmly adherent to the ciliary processes. From the sides of these processes fibres diverge at frequent intervals and pass to the margin of the lens, where they are attached on either side of the equator, spreading over a zone which is somewhat narrower posteriorly than anteriorly. These fibres form the suspensory ligament of the crystalline lens (Figs. 422 and 438). They occupy an annular zone which is included between the ciliary processes and the margin of the lens, and which is known as the *zonula of Zinn*.

The glassy fibres of this ligament take origin from the sides of the ciliary processes along which they are firmly attached, becoming free only near the apices of these processes. They pass thence to the margin of the lens and spread out upon the surface of the capsule to which they are intimately adherent.

The most anterior of these fibres form a somewhat plicated but incomplete membrane which serves as the anterior boundary of an annular series of connecting lymphatic spaces collectively forming the *spatia zonularis* (*canal of Petit*). This irregularly sacculated, annular canal is bounded posteriorly by the hyaloid membrane, anteriorly by the incomplete membranous wall of the posterior chamber through which the aqueous humor readily diffuses, internally by the margin of the crystalline lens, and antero-externally by the ciliary processes.

BLOOD VESSELS OF THE EYE

The circulation of blood in the globe of the eye is maintained through *four sets of vessels*:

1. The *arteria* and *vena centralis retinae*.
2. The short ciliary arteries and *venae vorticosae*.
3. The long ciliary arteries.
4. The anterior ciliary arteries and veins.

1. The **arteria centralis**, destined for the supply of the retina, enters the optic nerve about midway between the optic commissure

and the ocular globe, and arriving at the center of the nerve runs in its axis to the papilla optica, at which point it divides into two branches, which, by rapid dicotymous division, radiate from the optic papilla to all parts of the retinal surface, thereby forming a plexus of small arteries within the nerve fibre and ganglion cell layers. From this plexus capillaries are distributed to all the cerebral layers of the retina. No blood vessels are found within the neuro-epithelial layers. The retinal arteries, like those of the brain, do not anastomose with one another; they are terminal arteries.

The retinal veins follow a course exactly similar to that of the arteries; they converge to form a single efferent vessel, the vena centralis ratinæ. The retinal veins are peculiar in that their walls contain no muscle. The optic nerve is supplied

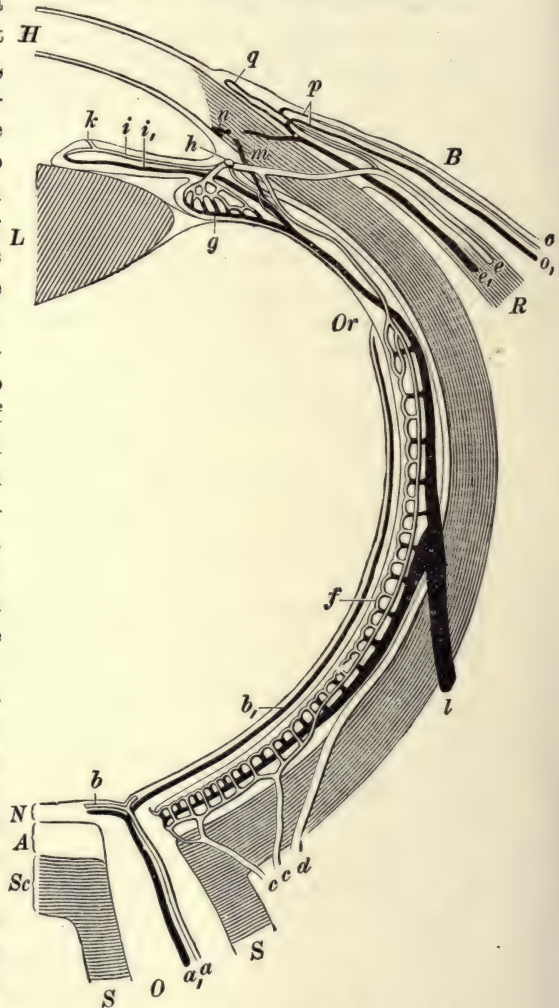


FIG. 439.—SCHEMATIC REPRESENTATION OF THE INTRINSIC BLOOD VESSELS OF THE EYE.

Arteries in outline, veins in solid black. A, choroid; a, central artery, and a₁, vein of the retina; B, conjunctiva; b, retinal arteries; b₁, retinal veins; c, c, short ciliary arteries; d, long ciliary artery; e, e₁, anterior ciliary arteries and veins; f, chorio-capillaris; g, capillaries of the ciliary body; H, cornea; h, circulus major of the iridal arteries; i, arteries, and i₁, veins of the iris; k, circulus minor of the iridal arteries; L, crystalline lens; l, venæ vorticosæ; m, anastomosis of ciliary and anterior ciliary veins; N, retina; n, canal of Schlemm; O, optic nerve; o, posterior conjunctival artery, and o₁, vein; p, anterior conjunctival vessels; q, vascular loops at the margin of the cornea; R, internal rectus muscle; S, sheath of the optic nerve; Sc, sclera. (After Leber.)

with small branches from the arteria and vena centralis retinae in their passage through its substance.

In the fetus a small branch, apparently the direct continuation of the arteria centralis retinae, passes forward through the vitreous humor to the posterior surface of the lens, whence capillary vessels pass around the margin of the lens and are connected with the anterior ciliary vessels at the margin of the iris. Before birth these vessels are occluded, their investing fibres remaining for a time as a minute fibrous canal, the *canalis hyaloideus* or *canal of Stilling*, which lies almost in the visual axis and extends from the papilla optica to the posterior surface of the lens. In adult life both the vitreous humor and the crystalline lens are bloodless tissues.

2. **The short ciliary arteries**, twelve to fifteen in number, enter the globe of the eye in a circle (*circle of Zinn*) which surrounds the optic nerve. They supply branches to the meningeal sheaths of the optic nerve and to the sclera, their main stems penetrating this coat to enter the choroid. Here they subdivide to form the plexus of arteries in the lamina vasculosa from which the vessels of the chorio-capillaris are supplied. The capillaries of the last-named layer unite to form small venous radicals which converge toward the equator of the eye, where they unite in a whorl-like manner to form the four or five *venæ vorticosæ*, which pass obliquely backward through the sclera, receiving additional branches from this coat, and finally emerging from the eye to empty into the ophthalmic vein.

The vessels of the choroid communicate posteriorly with those of the optic nerve, and anteriorly, by a free anastomosis, with those of the ciliary processes.

3. **The long ciliary arteries**, two in number, enter at the circle of Zinn on either side of the optic nerve, and pass horizontally forward upon the outer surface of the choroid to the ciliary muscle. Near the base of the iris they divide, and by anastomosis with each other and with the anterior ciliary arteries form a vascular circle, the *circulus major*, about the base of the iris.

From this circle recurrent branches supply the ciliary body and anastomose with the vessels of the choroid; other branches pass into the iris and, converging toward the visual axis form, just outside the pupillary margin, a second circle of anastomosis, the *circulus minor*.

The veins of the iris and ciliary body follow closely the distribution of the arteries, the greater portion of their blood return-

ing through the veins of the choroid and the *venae vorticosae*. Some, however, is returned by means of anastomoses with the anterior ciliary veins.

4. **The anterior ciliary arteries**, derived from the muscular and lachrymal branches of the ophthalmic, distribute branches to the conjunctiva and sclera, and within the latter membrane, about 2 mm. outside of the corneal margin, pass to the *circulus iridis major* and partially supply the iris and ciliary body as already described.

The anterior ciliary veins follow the course of the corresponding arteries. They empty into the vessels of the ocular conjunctiva.

THE LYMPHATIC SYSTEMS OF THE EYE.—The lymphatic systems of the eye include very few true lymphatic vessels, but rather consist of a series of channels which may be arbitrarily considered as an anterior and a posterior set of intercommunicating spaces. The former set includes the lymphatic spaces of the cornea, the spaces of Fontana, the anterior and posterior chambers, the lymphatic clefts of the ciliary muscle and iris, and the *spatia zonularis*. The posterior set includes the subdural and subarachnoid spaces in the sheath of the optic nerve, the capsule of Tenon, the lymphatic spaces of the lamina suprachoroidea, the perivascular spaces of the choroid and retina, the irregular clefts between the pigmentary and bacillary layers of the retina, the similar clefts of the ganglion cell layer, the lymphatic spaces of the hyaloid membrane, and the interstices of the vitreous humor.

These two sets of lymphatic channels communicate with each other by means of the perivascular spaces of the two outer tunics, as well as through that portion of the hyaloid membrane which forms the posterior wall of the *spatia zonularis*, through the clefts of which the lymph of the vitreous body communicates freely with the aqueous humor of the *spatia zonularis* and posterior chamber. Consequently, if the cornea be penetrated either accidentally or otherwise, and the anterior and posterior chambers be emptied, their aqueous humor is rapidly replaced, not only from the adjacent spaces of the anterior set of lymphatic vessels, but from the vitreous humor and posterior set as well.

It is also important to note that the posterior set of lymphatic spaces is directly connected through the meningeal sheaths of the optic nerve with the subdural and subarachnoid spaces of the cerebral meninges.

THE NERVES OF THE EYE.—The nerves of the eye, in addition to the optic, are the long and short ciliary. The former, two

or three in number, and the latter, six to ten, after supplying a vaso-motor branch to the arteria centralis retinae, pierce the sclera in company with the corresponding ciliary arteries and pass meridionally forward on the inner surface of the sclera, supplying branches to this tunic and to the vessels of the choroid, and finally reaching the ciliary muscle, where their branches form an annular plexus containing a few ganglion cells.

From this plexus fibrils are supplied to the blood vessels and muscular tissues of the ciliary body and iris, and to the cornea. The corneal branches pass to the annular plexus at the sclero-corneal junction, whence they are distributed to the corneal tissues, as already described (page 569).

APPENDAGES OF THE EYE

The appendages of the eye include the eyelids, conjunctiva, and lachrymal glands.

THE EYELIDS.—The eyelids are developed in the embryo as an invagination of the skin, which, leaving a slit-like aperture between its involuted margins, covers the inner surface of the lid to form the *palpebral conjunctiva*, and is reflected over the globe of the eye as the *ocular conjunctiva* and *anterior corneal epithelium*.

The lids, therefore, may be said to consist of two membranous portions, the cutaneous (outer or anterior) and the conjunctival (inner or posterior). Between these two portions the orbicularis palpebrarum forms a septum of striated muscle fibres.

The cutaneous portion of the eyelid differs from other portions of the skin only in that its subcutaneous tissue contains no fat. The derma is loosely connected with the muscle by a wide-meshed areolar tissue. Fine hairs are distributed over the cutaneous surface, their follicles extending well down through the derma. Small sebaceous glands open into the hair follicles and occasional sudoriparous glands pour their secretion upon the epidermal surface.

At the margin of the lid its cutaneous portion is reflected inward, and at its inner angle becomes directly continuous with the palpebral conjunctiva. The free margin of the lid presents, therefore, an *outer angle*, an *inner angle*, and an *intermediate surface*.

Two or three rows of large stiff hairs, the eyelashes, project from the outer angle, and large sebaceous glands open into their follicles. Other smaller sebaceous glands open directly upon the free surface.

The intermediate surface of the margin of the lid retains the character of the skin, though no hairs are found in this portion.

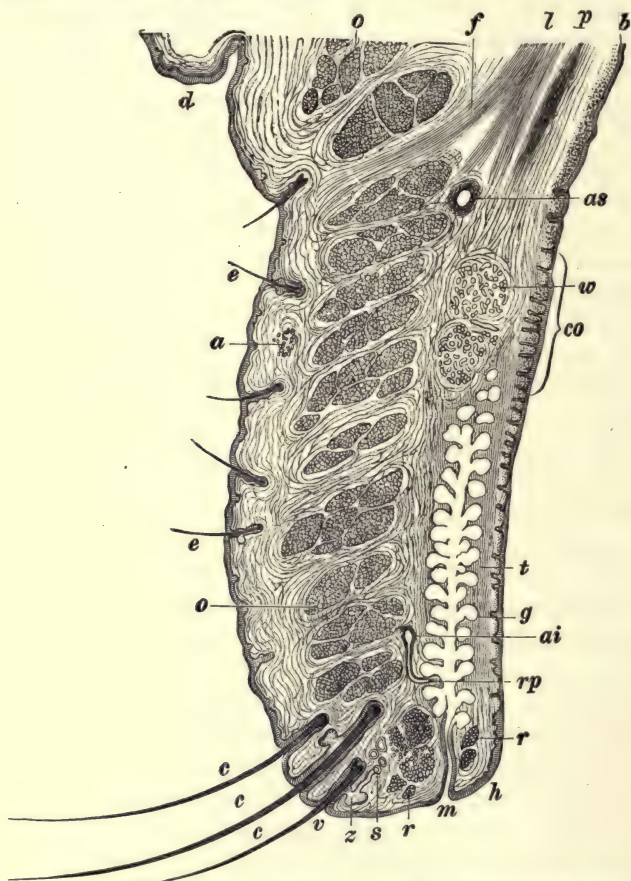


FIG. 440.—VERTICAL SECTION THROUGH THE UPPER EYELID.

a, sweat glands; *ai*, inferior arterial arch; *as*, superior arterial arch; *b*, conjunctival epithelium; *c*, eyelashes; *co*, rugated portion of the conjunctiva; *d*, epidermis; *e*, fine hairs; *f*, process of the levator palpebrae superioris which is inserted into the skin; *g*, Meibomian gland; *h*, internal angle of the margin of the lid; *l*, levator palpebrae superioris; *m*, duct of a Meibomian gland; *o*, orbicularis palpebrarum; *p*, superior palpebral muscle of Müller; *r*, ciliary muscle of Rioli; *s*, glands of Moll; *t*, fibrous tissue of the tarsus; *v*, external angle of the margin of the lid; *w*, posterior tarsal glands; *z*, sebaceous glands. (After Fuchs.)

Peculiar sweat glands, the *glands of Moll*, occur in the derma of this part.

At the inner angle of the lid the epidermis abruptly changes its

character to that of the conjunctiva, the derma of the cutaneous surface being continuous with the submucous connective tissue of this membrane. At the inner angle also, are the openings of the peculiar large sebaceous glands, the *tarsal glands of Meibom*, their orifices forming a continuous punctate row of pores barely visible to the naked eye.

The Meibomian glands are long compound saccular glands whose secreting saccules open into a common, axially placed duct which extends the whole length of the gland. Each saccule is filled with cells in various stages of fatty degeneration and is exactly similar in structure to the saccules of the ordinary sebaceous glands. The glands are embedded in the connective tissue of the conjunctiva and are so large as to form projecting ridges on its surface, which are disposed in vertical lines radiating from the row of glandular orifices at the margin of the lid. At their blind extremities the glands are often slightly bent or curved upon themselves, and this portion is embedded in a dense mass of fibrous tissue known as the *tarsus*.

The tarsus in each eyelid forms a very dense plate-like mass of areolar connective tissue which is so dense and resistant as to erroneously suggest a cartilaginous structure. It is inserted between the conjunctiva and the orbicularis muscle. It is thickest toward the free margin of the lid, but becomes progressively thinner in the opposite direction, until, as a mere fibrous membrane, the *palpebral fascia*, it is continued to the margin of the orbit.

The conjunctival portion of the lids, the *palpebral conjunctiva*, consists of a peculiar stratified epithelium and a thin connective tissue corium. Its epithelium comprises four or five layers of cells, the deeper of which are small and spheroidal, and the superficial elongated or conical, their blunt ends forming the free surface of the conjunctiva, their pointed extremities buried between the cells of the deeper layers. The bases of these elongated cells become somewhat expanded and broader from the increased tension of the conjunctiva when the lids are closed; they retract and become narrower when the lids are separated and the conjunctiva relaxed.

The cells of the superficial layer are often so distinctly elongated as to possess a columnar form. They may, however, be spheroidal or even somewhat flattened, in which case they very closely resemble the ordinary type of stratified squamous epithelium. The epithelial layer rests almost directly upon the connective tissue corium, the basement membrane being imperfectly developed.

The corium of the conjunctiva is thin. With the aid of a thin layer of submucous areolar tissue it unites the epithelium to the tarsus and to the fibres of the orbicularis muscle; near the margin of the lid its submucous tissue incloses the Meibomian glands. Opposite the plane at which the blind ends of the Meibomian glands are embedded in the free margin of the tarsus, the conjunctival surface is thrown into eight to twelve horizontal folds, beneath which, in the connective tissue, are a few minute tubulo-alveolar glands, the *posterior tarsal glands (glands of Waldeyer)*. Their ducts open upon the free surface of the conjunctiva near the fornix conjunctivae.

At the attached base of the lid a narrow band of smooth muscle extends from the levator palpebrae and inferior oblique muscles into the body of the lid. These fibres have been described by H. Müller* as the superior and inferior *palpebral muscle* of the upper and lower lid, respectively.

The fold by which the palpebral conjunctiva is reflected upon the globe of the eye to become continuous with the ocular portion of the membrane is known as the *fornix conjunctivae*. The extremely loose attachment of the conjunctiva of the fornix to the underlying connective tissue and intraorbital fat permits the great freedom of motion which is characteristic of the ocular globe. The small *accessory lachrymal gland (gland of Krause)* opens into the margin of the fornix conjunctivae. In this region, also, occasional goblet cells occur in the superficial layers of the epithelium.

The ocular conjunctiva is likewise very loosely attached to the sclera. The scleral portion of the conjunctiva is nearly identical in structure with the palpebral portion already described. Near the margin of the cornea the superficial cells of the epithelium become at first spheroidal and then, as the cornea is approached, they are progressively flattened, so that, just outside of the corneal margin, the conjunctival epithelium conforms to the stratified squamous type which forms the anterior epithelium of the cornea.

THE LACHRYMAL GLAND.—The lachrymal glands are two flattened, lobulated, glandular masses situated at the upper and outer angle of the orbit, one in relation with each eye. They secrete a clear watery fluid, the tears. These glands are somewhat moulded to conform to the shape of the orbit and the globe of the eye, between which they are inserted.

Each lachrymal gland is a secreting gland of the compound

* Sitz. d. phys. med. Gesellsch., Würzburg, 1858.

tubular type (Marziarski*) (Fig. 174, page 192), and consists of eight to twelve small lobules which open into the fornix conjunctivae by about as many minute ducts. The lobules are united by thin fibrous fasciae which contain the larger ducts.

Each lobule of the gland contains many serous secreting acini and numerous small intralobular ducts. The secreting acini are



FIG. 441.—SECTION THROUGH A LOBULE OF THE LACHRYMAL GLAND OF MAN.

a, small duct branching within the lobule; *b*, intercalary ducts; *c*, connective tissue; *f*, fat cells. *A*, transection of an interlobular duct. Hematoxylin and eosin. $\times 112$. (After Kölliker.)

lined by tall, columnar cells, resting upon a thin basement membrane, which is supplied with basket cells (*Korbzellen*) and is invested with a delicate fibrous tunica propria. The appearance of the secreting epithelium differs somewhat according to its state of activity. After a period of rest, and in the ordinary condition of relative inactivity, the epithelium becomes distended with secretion and is either clear in appearance or at most is only very finely granular, the nuclei are crowded to the base of the swollen cells,

* Anat. Hefte, 1901.

and the lumen of the acinus is very small. After a period of excessive activity the secreting cells become shrunken and more distinctly granular, and the lumen of the acinus appears much dilated.

The secreting acini empty into narrow *intercalated ducts* which lie within the lobule, have a considerable lumen, and are lined by tall columnar cells resting upon a second incomplete layer of small, somewhat flattened basket cells.

These *intralobular ducts* unite at the margin of the lobule to form the larger *interlobular ducts*, which are contained in the interlobular connective tissue. Here the duct is lined by low columnar or even somewhat flattened cells, at first disposed in a single, but later in a double layer. As the duct approaches the conjunctival surface the number of cell layers increases until their lining epithelium finally comes to resemble the stratified epithelium of the conjunctiva with which it is continuous.

Minute collections of diffuse lymphoid tissue and even small lymphatic nodules are occasionally found just beneath the epithelium of the conjunctiva in the neighborhood of the lachrymal glands of the fornix; occasionally the lymphoid tissue is quite abundant.

In mammals possessing a *membrana nictitans* ("third lid") a small, mucus secreting gland occurs at the inner angle of the orbit; this is known as the *gland of Harder*. In man it is usually absent, though in an extremely vestigial condition it may occasionally be found.

CHAPTER XXIX

THE EAR

THIS organ may be subdivided for description into the external, the middle, and the internal ear. The first two portions serve for the collection and transmission of sound waves, the last for the transformation of the sound waves into nerve stimuli which are then transmitted through the path of the auditory nerve to the cerebrum.

THE EXTERNAL EAR

The external ear includes an auricular or free portion and an external auditory canal.

THE AURICLE contains a thin cartilaginous plate of peculiar form which is covered on both sides by the skin. The cartilage is of the elastic variety, but differs from the similar cartilages of other parts in the abundance of its large cartilage cells; in occasional areas the elastic reticulum is deficient. This reticulum is closely connected with the fibrous perichondrium, beneath which it forms a complete layer. The extrinsic muscles of the ear are inserted into the perichondrium and the fibrous tissue by which it is surrounded.

The skin of the external ear does not essentially differ from that of other parts. It is supplied with fine hairs and with many large sebaceous glands; sweat glands also occur on the outer surface. The derma is united to the underlying cartilage by connective tissue; on the concave surface this union is very firm and permits but little motion. The subcutaneous tissue, except in the lobule, contains but little fat.

THE EXTERNAL AUDITORY CANAL is divisible into an outer cartilaginous and an inner bony portion; the walls of the two portions, except for this difference, are quite similar in structure. The cartilage is continuous with that of the auricle, and is of the cellular elastic variety. The skin of this portion contains large stiff hairs and both sebaceous and ceruminous glands. The

former, as in the auricle, open either upon the free surface of the skin or into the adjacent portion of the hair follicles.

The ceruminous glands resemble in structure the sweat glands of other portions. They are coiled tubular glands which open



FIG. 442.—TRANSECTION OF THE LOBULE OF THE EXTERNAL EAR OF AN INFANT.
a, cartilage; *b*, skin; *c*, adipose connective tissue. Hematein and eosin. Photo. $\times 20$.

upon the surface of the skin by means of a narrow duct. The coils of their secreting portion are lined by columnar cells with spheroidal, basally situated nuclei and a clear cytoplasm containing many small brownish granules of pigment and a few fatty particles. The cytoplasm is often diffusely colored by the brownish pigment. The secretion of these glands, the cerumen, in addition to the pig-

mented and fatty secretion of the glands, contains desquamated epithelial cells and occasional fine hairs, together with foreign particles of a very varied sort.

In the bony portion of the canal the corium or derma is firmly adherent to the periosteum of the bone, and all the layers of the skin are much reduced in thickness. The scanty hairs are very fine, and, with the glands, are continued inward to the tympanic membrane only in the superior portion of the wall of the canal.

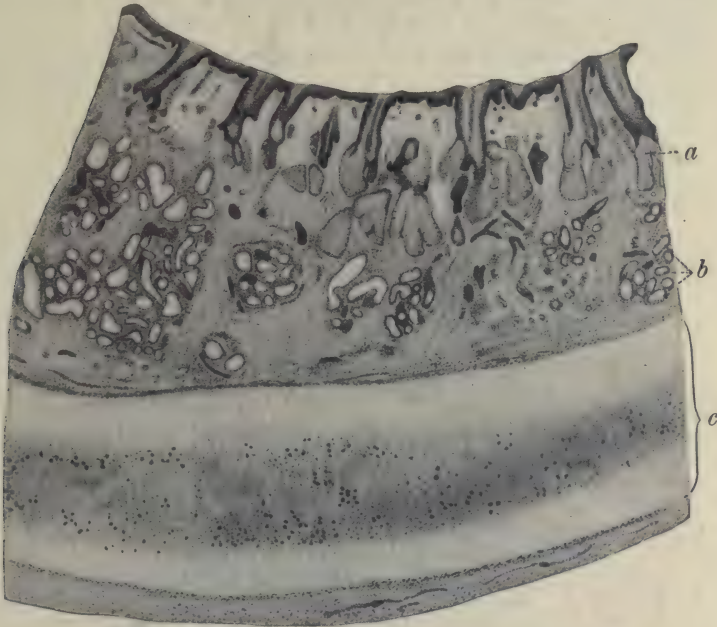


FIG. 443.—FROM THE EXTERNAL AUDITORY CANAL OF MAN.

a, sebaceous gland; *b*, ceruminous gland; *c*, cartilage. Hematoxylin and eosin. $\times 15$.
(After Sobotta.)

Papillae are present as far as the margin of the drum membrane. Upon the surface of the tympanic or drum membrane, which closes the inner end of the external auditory canal and separates it from the cavity of the middle ear, the skin is reduced to an extremely thin cutaneous coat, devoid of hairs, glands, and papillae.

THE MIDDLE EAR

The middle ear or *tympanum* is an irregular cavity, broad above and behind, narrow below and in front, which lies just

within the external auditory canal. Its outer wall is largely formed by the tympanic or drum membrane, its inner by the osseous wall of the internal ear.

The contour of the tympanum is very irregular, its cavity being encroached upon by numerous bony indentations which are most pronounced in its internal wall. Externally the tympanic membrane is attached to a bony and fibro-cartilaginous ring, the *annulus tympanicus*, which projects somewhat into the tympanic cavity. In front, the orifice of the Eustachian tube is marked by a slight cartilaginous projection near the floor of the cavity.

Above and behind, the tympanic cavity is prolonged into a deep recess, the *epitympanic cavity*, in the upper part of whose posterior



FIG. 444.—FROM A SECTION OF THE MIDDLE AND INTERNAL EAR OF A GUINEA-PIG.

Near *x* is the inner portion of the external auditory meatus in longitudinal section; it is closed by the delicate drum membrane. At the left of the drum membrane within the tympanum is the incus approaching its articulation with the stapes, one arm and the base of which are shown. The base of the stapes, in the foramen ovalis, is directed toward the vestibule, in which sections of the utricle and saccule are seen. The facial nerve lies at the left of the stapes. Hematein and eosin. Photo. $\times 9$.

wall are the orifices of the mastoid cells. The upper portion of the cavity contains the rounded heads of the malleus and incus, the two largest of the auditory ossicles. The internal wall of the tympanum presents anteriorly a bulging prominence which is known as the

promontory, and which indicates the position of the first or broadest turn of the spiral canal of the cochlea. Beneath this prominence is a recess leading to a bony "window," the *fenestra rotunda*, which, in life, is closed by a delicate membrane. Behind the promontory and at a slightly higher level a deep recess, the *pelvis ovalis*, leads inward to the *fenestra ovalis*, which is closed by the base of the stapes; the body of this ossicle is entirely contained within the pelvic recess, and near its mouth the stapes articulates with the orbicular extremity of the long process of the incus. The superior portion of this deep recess is encroached upon by the projecting wall of the *aqueductus Fallopii* which transmits the *facial nerve*, and posteriorly, near the point where it merges with the general tympanic cavity, a low, conical, bony projection known as the *pyramid* transmits the *stapedius muscle*. The canal of the *tensor tympani muscle* contained within a still more prominent, conical, bony projection, the *processus cochleariformis*, is found near the antero-internal angle of the tympanic cavity just above and parallel to the Eustachian tube. The narrowest portion of the tympanum is, perhaps, almost its very center, and is included between the promontory on the inner and the tympanic membrane on the outer side. Extending from this narrowed central portion upward, backward, and inward, are expanded recesses which are partially occupied by the three auditory ossicles; the remaining portions of the tympanum are filled by air which gains access to the cavity through the Eustachian tube.

The tympanic mucosa consists of a thin but dense tunica propria which is firmly attached to the underlying periosteum and softer parts by loose connective tissue, and is clothed with a layer of flattened epithelium, which, in the vicinity of the origin of the Eustachian tube, is of low columnar form and is provided with cilia, but in most other portions of the tympanum is squamous in character and of the tessellated type, closely resembling endothelium. The floor of the tympanum and the lower portions of its anterior, internal, and posterior walls also possesses a partial clothing of low ciliated cells (Kessel*). Occasional gland-like folds of the mucosa occur near the orifice of the Eustachian tube, though the true glandular character of these folds is very questionable.

The mastoid cells are numerous small spaces situated within the mastoid process of the temporal bone; they are lined by a continuation of the tympanic mucosa, which is everywhere clothed by flat-

* Stricker's Handbook, vol. iii.

tened epithelium. The chorium is closely attached to the periosteum of the bony wall, the periosteum also serving as a vascular layer of the mucosa in the mastoid cells, as well as in the general tympanic cavity.

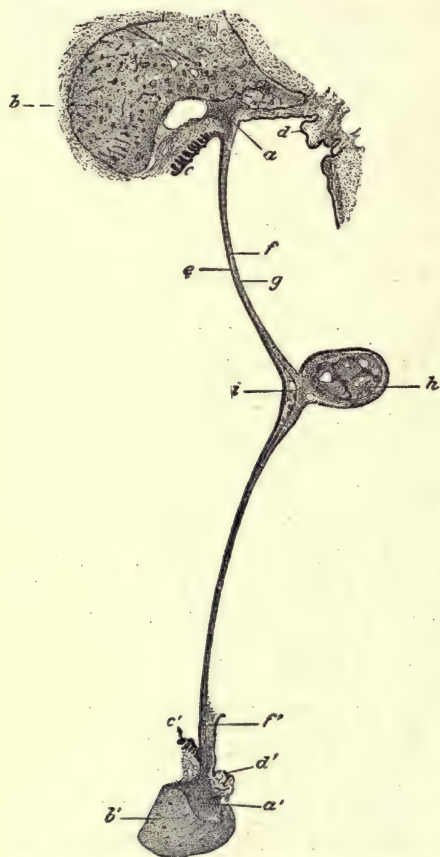


FIG. 445.—TRANSECTION OF THE TYMPANIC MEMBRANE OF A CHILD.

a, a', fibro-cartilaginous ring; *b, b'*, bone; *c, c'*, skin of the external auditory canal; *d, d'*, tympanic mucosa; *e*, cutaneous layer of the tympanic mucosa; *f*, fibrous layer, obliquely cut at *f'*; *g*, layer derived from the tympanic mucosa; *h*, handle of the malleus; *i*, blood vessels. Hematoxylin and eosin. $\times 11$. (After Kölliker.)

The tympanic membrane is a thin delicate partition which is formed by a reflection of the cutaneous layer of the external auditory canal on the one hand, the tympanic mucosa on the other, and between these two membranes a layer of dense fibrous tissue whose tendinous bands are disposed in radial and circular directions. The margin of the tympanic membrane is inserted into a fibro-cartilaginous ring which rests upon a bony elevation, the *annulus tympanicus*.

The slender manubrium or handle of the malleus projects from the superior margin of the ring and is inserted between the folds of the tympanic membrane, extending downward to about the center of the membrane, at which point is the deepest part of its concavity, its *umbo*. The bony handle of the malleus, lying between the cutaneous and mucous layers of the tympanic membrane, is covered

by a thin cartilaginous layer, and receives the insertions of the tendinous fibres. These fibres are divisible into an outer radial layer which extends from the fibro-cartilaginous ring at the periph-

ery inward to the manubrium mallei, and an inner circular layer whose thickest portions are found close to the manubrium and near the periphery of the membrane; between these points the circular layer of fibres is partially or entirely deficient. Just within the fibro-cartilaginous ring at the periphery of the membrane the circular layer of fibres abruptly ends.

The cutaneous layer of the tympanic membrane forms a very thin coat, its epidermis consisting of a Malpighian layer one or two cells deep, which is covered by several flattened non-nucleated cells of the horny portion. The derma or corium is very thin, contains no papillae, and is intimately adherent to the fibrous layers of the membrane; it contains neither glands nor hairs.

The mucous layer of the tympanic membrane is even thinner than the cutaneous. It consists of a flattened epithelium which rests almost directly upon the layer of circular fibres. A few connective tissue fibres pass irregularly from the mucous, through the fibrous, to the cutaneous layer, thus firmly uniting the several layers into a compact membrane.

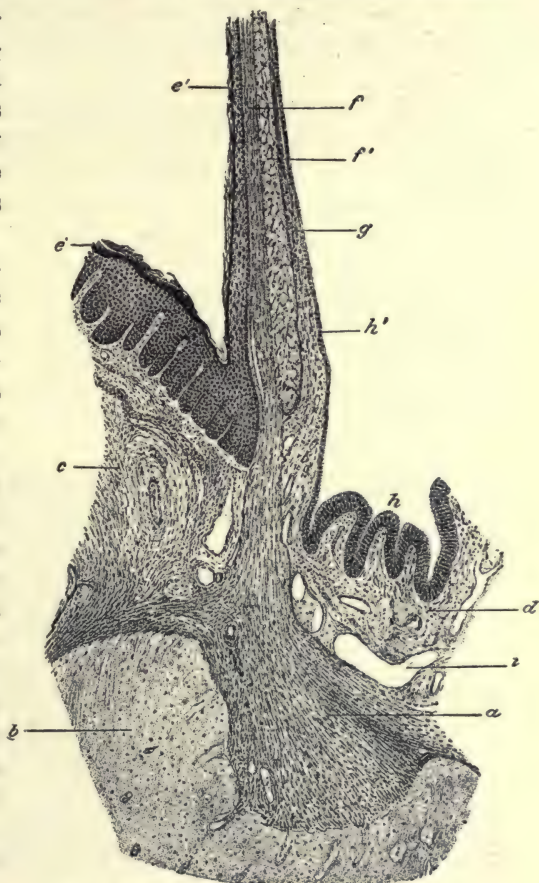


FIG. 446.—SECTION THROUGH THE MARGIN OF THE TYMPANIC MEMBRANE OF A CHILD.

a, fibro-cartilaginous ring; *b*, bone; *c*, derma of the external auditory canal; *d*, tympanic mucosa; *e*, *e'*, epidermis; *f*, radial fibres, and *f'*, circular fibres of the tympanic membrane; *g*, mucosa of the membrane; *h*, epithelium of the tympanum; *i*, blood vessels. $\times 55$. (After Kölliker.)

In the upper quadrant of the tympanic membrane, above the attachment of the malleus, the fibrous layers are wanting; the mucous and cutaneous layers are therefore in contact, and the membrane presents a flaccid appearance in comparison with the tense condition of its other parts. This portion is known as *Shrapnell's membrane*.

The Auditory Ossicles.—These are three in number, the malleus, the incus, and the stapes; they form a continuous bony chain, extending from the insertion of the manubrium mallei in the tympanic membrane to the fenestra ovalis, with whose margin the foot of the stapes articulates. The ossicles consist of compact bony tissue containing loosely packed Haversian systems; they are united with each other by firm fibro-cartilaginous articulations. With the exception of the stapes, none of the ossicles contain a marrow cavity.

The manubrium of the malleus is firmly fixed in the tympanic membrane, as already described, the head of the bone articulating

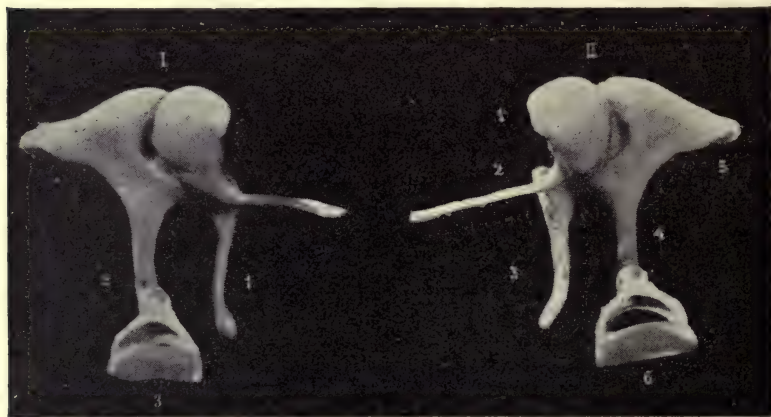


FIG. 447.—THE AUDITORY OSSICLES.

I, ossicular chain of the left ear; 1, malleus; 2, incus; 3, stapes. *II*, ossicular chain of the right ear; 1, malleus; 2, processus gracilis; 3, manubrium; 4, long process of the incus; 5, short process of the incus; 6, stapes. (After Rüdinger.)

with the head of the incus in the epitympanic recess. The long process of the incus, circular in transection, extends downward along the tympanic wall in a course nearly parallel to that of the manubrium mallei, being, in a portion of its course, contained within a recess in the osseous wall of the tympanum. Finally, at the level of the stapes it makes a sharp bend, almost at right angles

with its former course, to articulate, by means of a rounded end or *orbicular process*, with the head of the stapes. This latter bone is deeply placed within the recess of the pelvis ovalis, and continues the bony chain to the fenestra ovalis, where the foot plate of the stapes is in relation, by its inner surface, with the vestibular perilymphatic space of the internal ear.

The course of the chain of ossicles is such that they form a lever; the long process of the incus being shorter than the manubrium mallei, the vibrations of the tympanic membrane in response to sound waves are transmitted to the internal ear diminished in amplitude but exaggerated in intensity.

Two muscles and several ligaments are connected with the ossicles.

The tensor tympani muscle is mostly contained within a canal which is parallel to and lies just above the Eustachian tube, and from its bony wall the muscular fibres arise. The wall of the canal forms a conical projection known as the *processus cochleariformis*, which projects

well into the cavity of the tympanum, being directed toward the neck of the malleus. Leaving its canal at the apex of this conical process the tendon of the muscle bends sharply over the margin of the *processus cochleariformis* and passes directly to its insertion into the neck and the adjoining part of the manubrium of the malleus. Hence the naked tendon of the muscle lies within the tympanic cavity.

The stapedius muscle is similarly contained within the cavity of the pyramid, from whose bony wall its fibres take origin. Passing forward, the muscle makes its exit at the apex of the pyramid,

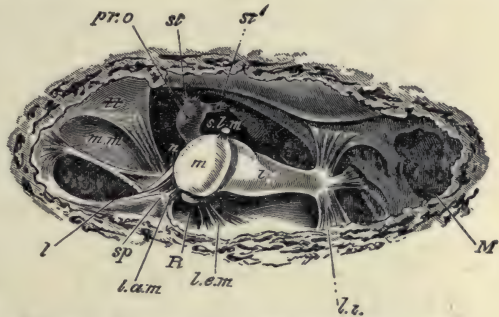


FIG. 448.—THE CAVITY OF THE TYMPANUM, VIEWED FROM ABOVE.

i, the body of the incus; *l*, ligamentous fold of the mucosa; *l.a.m.*, anterior ligament of the malleus; *l.e.m.*, external ligament of the malleus; *l.i.*, posterior ligament of the incus; *M*, mastoid cell; *m*, head of the malleus; *m.m.*, mucous membrane; *n*, chorda tympani nerve; *pr.o.*, orbicular process of the incus articulating with the stapes in the depth of the cavity; *R*, beneath this space is the flaccid portion of the tympanic membrane; *s.l.m.*, cut end of the superior ligament of the malleus; *sp*, spina tympanica anterior; *st, st'*, tendon of the stapedius muscle; *tt*, tendon of the tensor tympani muscle. $\times 4$. (After Schäfer.)

and is directly inserted into the neck of the stapes close to the articulation of the orbicular process of the incus.

The ligaments of the malleus are the anterior, the external, and the superior. The anterior ligament firmly attaches the head of the malleus to the margin of the Glasserian fissure in the anterior wall of the tympanum. The processus gracilis of the malleus is inclosed by the fibres of this ligament. It is also in close relation with the chorda tympani, which, being clothed by the tympanic mucosa, traverses this portion of the tympanic cavity and enters the iter chordae anterioris.

The external ligament connects the neck of the malleus with the upper portion of the external wall of the tympanum. It is somewhat fan-shaped. The superior ligament is a looser fibrous band which passes from the head of the malleus to the superior wall of the tympanum.

The ligament of the incus is decidedly fan-shaped, its straight, coarse, fibrous bands radiating from the short process of the ossicle to the adjacent portion of the posterior wall of the tympanum.

The articulation of the malleus with the incus, as also that of the latter bone with the stapes, is supplied with a delicate capsular ligament.

The annular ligament of the stapes connects the margin of the foot plate of this bone with the adjacent portions of the cartilaginous and bony wall of the vestibule at the margin of the fenestra ovalis. The articulation which is thus inclosed is directly formed by an annular plate of cartilage investing the margin of the oval foot of the stapes, and a similar annular plate of hyaline cartilage which lines the borders of the foramen ovalis. The fibres of the annular ligament are continuous with those of the perichondrium and adjacent periosteum.

THE EUSTACHIAN TUBE

The Eustachian tube connects the cavity of the tympanum with that of the naso-pharynx. Its first portion is surrounded by a bony wall; beyond this it is supplied with a cartilaginous plate; its pharyngeal ostium is entirely membranous.

The mucosa consists of an epithelium, which is of the columnar ciliated variety, continuous with, and similar to the respiratory epithelium of the naso-pharynx, together with a fibrous membrana propria which is loosely connected with the surrounding bony, cartilaginous, and muscular walls. The lower portions of the tube are

richly supplied with mucus secreting, tubulo-acinar glands, and toward its pharyngeal end the mucosa is much infiltrated with lymphoid tissue, thus forming the *tubal tonsil* of Gerlach.

The cartilage of the Eustachian tube is firmly adherent to the bony wall. At the point of attachment it has a hyaline structure,



FIG. 449.—TRANSECTION OF THE EUSTACHIAN TUBE; DIAGRAMMATIC.

1, cartilaginous plate; 2, median or hooked end of the cartilage; 3, "dilator tubae"; 4, levator palati; 5, fibrocartilage at the base of the skull; 6 and 7, mucous glands; 8, adipose tissue; 9, 11, lumen of the tube; 10, 12, connective tissue. Low magnification. (After Rüdinger.)

the fibres of the perichondrium penetrating only the surface of the cartilaginous plate. Lower down the cartilage becomes infiltrated with fibres and conforms to the typical elastic or reticular variety. Like the cartilage of the auricle it is rich in cellular elements. Its transection presents a peculiar hook-like form, by means of which the posterior surface, the superior margin, and the upper portion of the anterior surface are invested by cartilage, while the remaining portions of the anterior surface and the whole of the inferior margin are entirely membranous.

VASCULAR SUPPLY.—The mucosa of the middle ear is richly supplied with blood vessels, the larger of which lie in the deeper

part of the membrane and supply capillary vessels to the tunica propria. The blood vessels of the Eustachian tube are especially numerous.

In the tympanic membrane the arteries and veins form an annular plexus at the margin; and a group of similar vessels surrounds the manubrium mallei, lying in the deeper layers of the cutaneous portion of the membrane.

The mucosa of the tympanum is peculiar in the relative deficiency of capillary vessels (Prussak*); the veins are numerous. The veins of the Eustachian tube empty into the internal jugular; they also communicate with the cavernous sinus by a trunk of considerable size (Dench †).

The lymphatics of the middle ear form plexuses in the connective tissue of the mucosa and in a general way follow the course of the smaller veins. They lead in part to the lymphatic nodes behind the ear, and in part to the parotid group (Kölliker ‡). They also communicate with the perilymphatic spaces of the internal ear.

THE INTERNAL EAR

The internal ear includes a series of membranous structures together with the terminal apparatus of the eighth cranial nerve; these are contained within a series of connected cavities hollowed out of the petrous portion of the temporal bone, they are in relation with the mesial wall of the tympanum. The central portion of this bony cavity, an ovoid space, is known as the vestibule; its outer wall presents the orifice of the fenestra ovalis which leads to the tympanum, but during life is closed by the base of the stapes. Opening from the vestibule, on the one hand, are the bony cavities occupied by the three semicircular canals which, in a general way, project from the dorsal aspect of the vestibule; on the other hand the bony cochlea containing its series of spiral canals projects anteriorly from the vestibule. Collectively these spaces, with several diverticula, form the *bony labyrinth*, and within them in life are contained a number of membranous sacs whose general form corresponds more or less closely to that of the bony cavity; these sacs collectively form the *membranous labyrinth*.

The vestibule contains two of these membranous sacs, the *sacculus* and the *utricle*, which are connected by means of the slender

* Arch. f. Ohrenheilk., 1869.

† Diseases of the Ear, 1895.

‡ Handbuch, III.

utrículo-saccular canal, from which a much prolonged diverticulum enters the aqueductus vestibuli to penetrate to the posterior surface of the petrous bone where it comes into relation with the cerebral meninges; this diverticulum is known as the *ductus endolymphaticus*. The utricle and saccule, as also all other portions of the

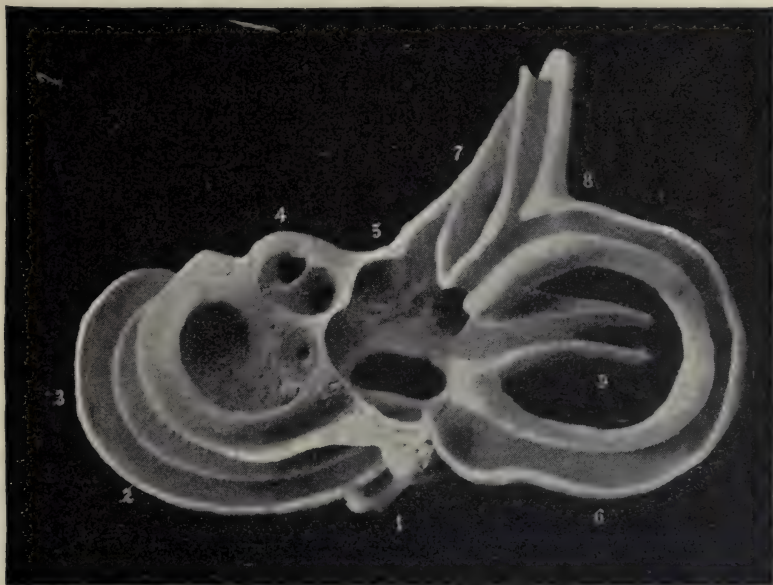


FIG. 450.—THE BONY LABYRINTH.

1, round window; 2, osseous lamina spiralis; 3, osseous cochlear canal; 4, floor of internal auditory meatus; 5, vestibule; 6, 7, 8, 9, semicircular canals. The figures are placed at that portion of the margin which is nearest the structure indicated. (After Rüdinger.)

membranous labyrinth, contain a watery fluid, the *endolymph*; they do not entirely fill the bony cavity of the labyrinth in which they lie, the intervening space being occupied by a retiform connective tissue with broad interstices which are permeated by an aqueous fluid, the *perilymph*.

The saccule is a rounded membranous cavity which is connected, on the one hand, by means of the slender *canalis reuniens*, with the cochlear duct or scala media, and on the other hand with the ductus endolymphaticus and utricle, as already stated. Its wall consists of an endothelium, a membrana propria and a fibrous coat. The endothelium consists of flattened squamous cells; it completely lines the cavity. The epithelial surface is somewhat irreg-

ular from the papillary elevations of the fibrous coat. On the antero-inferior surface of the saccule the epithelium is peculiarly altered so as to form a layer of columnar cells, many of which are provided with cilia. This *neuro-epithelium* is distributed over an oval area beneath which the fibrous coat is much thickened by the entrance of many fibres derived from the vestibular nerve. This elevation with its neuro-epithelial covering is known as the *macula sacculi*.

The neuro-epithelium contains two varieties of cells, the *sustentacular* and the *hair cells*. The former, *fibre cells* of Retzius,

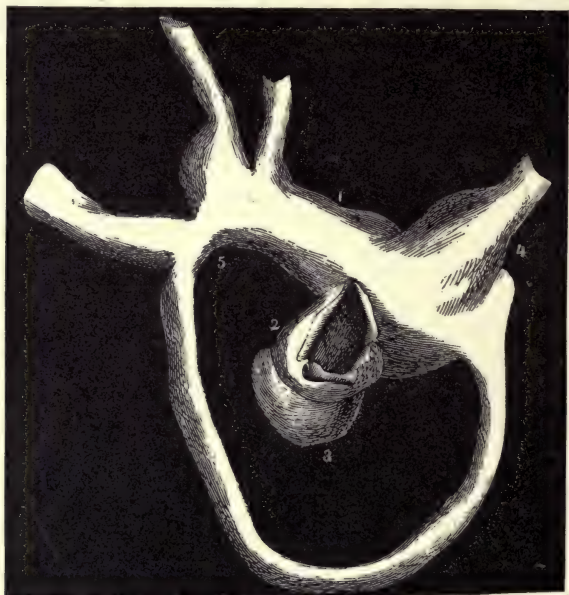


FIG. 451.—THE ISOLATED MEMBRANOUS LABYRINTH.

1, utricle; 2, saccule (opened); 3, location of the macula sacculi; 4, ampulla of a semi-circular canal; 5, canalis communis. Low magnification. (After Rüdinger.)

form a layer, two or three cells deep, which rests upon the basement membrane, and whose broad basal portion contains a spheroidal nucleus. Beyond the nucleated portion the cytoplasm of the sustentacular cell is continued inward between the bodies of the hair cells to the surface of the epithelial layer, this portion of the cell being relatively slender.

The hair cells occupy the superficial part of the epithelial layer by their broad nucleated portions, which carry upon their free

extremity a single tuft of long cilia, having the appearance of a delicate hair-like process which projects into the endolymphatic cavity. That portion of the endolymph which immediately over-

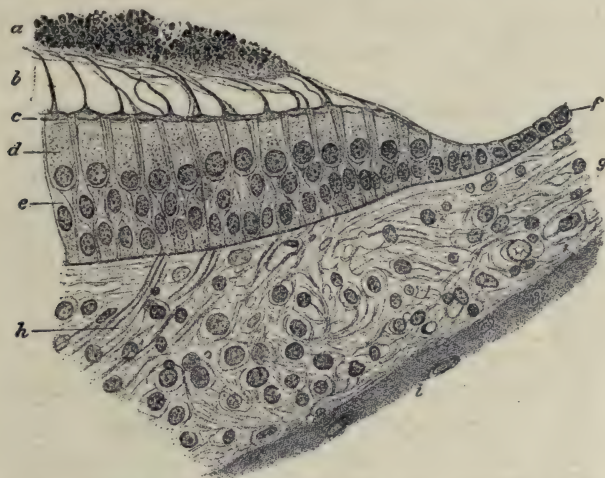


FIG. 452.—TRANSECTION OF THE MARGIN OF THE MACULA SACCULI OF A GUINEA-FIG.

a, otolithic membrane; *b*, cilia; *c*, cuticular membrane; *d*, hair cells; *e*, sustentacular cells; *f*, epithelium of the saccule; *g*, tunica propria; *h*, nerve fibres; *i*, bone. Hematoxylin and eosin. $\times 325$. (After K  lliker.)

lies the macula, and into which the hair-like processes project, though not essentially different in microscopic appearance in fresh tissues, appears to possess a somewhat gelatinous consistence, and in it are suspended various forms of crystals of calcium carbonate which are known as *otoliths*. The free surface of the neuro-epithelium is also provided with a reticulated cuticular membrane which presumably is formed by the amalgamation of the free ends of the sustentacular cells. Through the openings in this reticular membrane the ciliary tufts of the hair cells project.

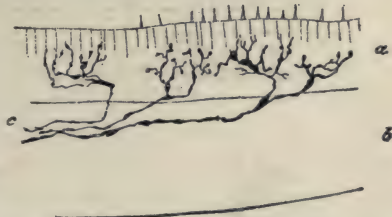


FIG. 453.—NERVE ENDINGS IN THE MACULA OF A GUINEA-FIG.

a, epithelium; *b*, tunica propria; *c*, three terminal nerve fibres. Golgi stain. \times about 200. (After Retzius.)

The central ends of the hair cells, beneath the nucleated enlargement which is found near the middle of the epithelial layer,

are prolonged outward between the nucleated portions of the sustentacular cells and frequently terminate in small knobbed extremities. This portion of the cells is in intimate relation with the terminal fibrils of the vestibular nerve, which, coming from nerve plexus in the fibrous wall of the saccule, forms an intra-epithelial plexus of delicate varicose fibrils. Frequently the epithelial coat contains coarse granules of a brownish pigment which, at times, also produces a diffuse coloration of the cells.

The epithelial coat of the saccule rests upon a thin homogeneous basement membrane and is further supported by a delicate fibrous coat or tunica propria. The connective tissue of this coat forms interlacing bundles the most of which are distributed in a circular manner about the wall of the ovoid saccule. At the macula this coat is much thickened by the entrance of the nerve fibres from the vestibular nerve. It also contains the minute blood vessels which supply the organ.

As is the case with the other divisions of the membranous labyrinth, the fibrous wall of the saccule is in contact on one aspect of its surface with the periosteum which lines the osseous labyrinth; elsewhere it is separated from the periosteum by the perilymphatic cavity.

The utricle is somewhat larger than the saccule. It lies behind and somewhat above the saccule, is of a very irregular oblong form, and receives the insertions of the semicircular canals. Its anterior portion is provided with a macula and the structure of its wall differs in no wise from that of the saccule; both of these membranous sacs are contained within the irregular cavity of the vestibule. The structure of the utricle, therefore, requires no further description.

The Semicircular Canals.—The semicircular canals are three in number, the posterior, superior, and external. The last is also horizontal in its position; the first two are vertical, but are so placed as to form a right angle with one another. The superior lies in the long axis of the petrous bone and its plane is therefore more nearly coronal, while that of the posterior canal is more nearly sagittal. Each canal forms something more than half a circle, its two ends opening separately into the cavity of the vestibule, with the exception of the posterior and superior canals whose inserted ends open by a common orifice, the *canalis communis*. The unjoined orifices of the posterior and superior canals, as also the outer extremity of the external canal, present a marked dila-

tation at their termination in the vestibule. These dilatations are known as the ampullæ. The osseous and membranous canals are of similar shape; the latter is, of course, contained within the former.

The membranous semicircular canals open into the utricle. They do not entirely fill their bony canal, but, like the utricle and

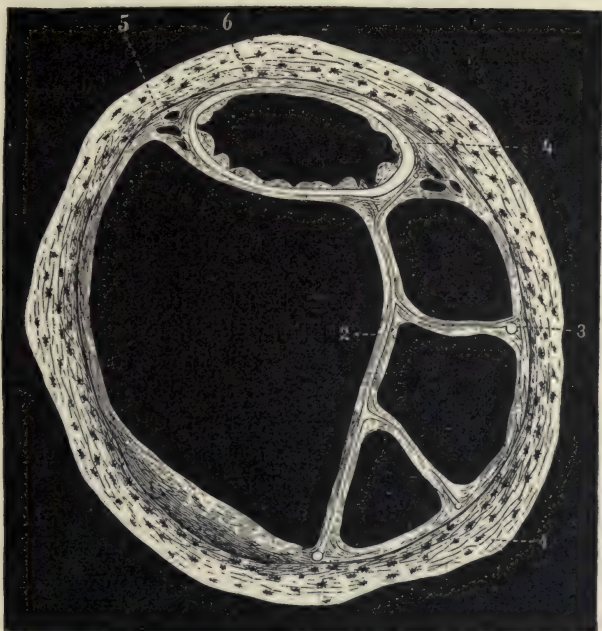


FIG. 454.—TRANSECTION OF A HUMAN SEMICIRCULAR CANAL.

1, bone; 2, retiform connective tissue membranes; 3, at this point a band of connective tissue joins the periosteum; 4, membranous semicircular canal; 5, ligamentous attachment of the canal; 6, at this point the membranous and osseous canals are in contact. Moderately magnified. (After Rüdinger.)

sacculæ, lie in contact with the periosteum at one surface only, this surface being that of the outer wall or periphery of the semicircle, while in the remaining portion of the circumference of the cylindrical bony canal, the membranous canal is loosely united to the periosteum of the osseous wall by a retiform connective tissue whose loose meshes are filled with perilymph.

The wall of the membranous canal is similar in structure to that of the sacculæ and utricle and consists of an endothelium, a membrana propria, and a fibrous tunic. Each of the three ampullæ

presents a marked differentiation of the epithelial lining, which is there raised in the form of a prominent crescentic fold, falsely termed by the older anatomists the *crista acustica*, from its supposed connection with the auditory function. Like the maculae of the saccule and utricle, the cristae are supplied by the vestibular nerve and are concerned with the function of equilibration.

The cristae are clothed with tall columnar cells which, though somewhat taller, are otherwise similar in structure to those of the maculae, and are similarly divisible into sustentacular cells and hair cells. They are also covered by a gelatinous cuticular formation, containing otoliths, which is here known as the *cupola*.

THE COCHLEA

The cochlea, like the vestibular portion of the internal ear, consists of a bony case which incloses a series of spiral membranous canals.

The bony cochlea possesses a peculiar pyramidal shape. The base of the pyramid is in contact with the anterior aspect of the

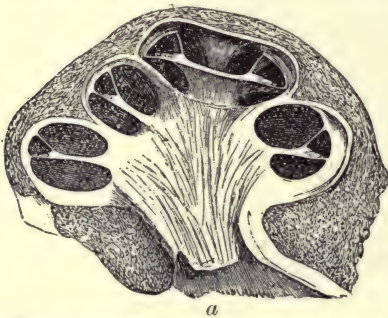


FIG. 455.—AXIAL SECTION THROUGH THE COCHLEA OF A FETAL CALF.

a, internal auditory meatus in which is the cut end of the cochlear nerve as it enters the modiolus. $\times 6$. (After Köl liker.)

vestibule; its apex or *cupola* is directed forward, outward, and slightly downward. The pyramid is hollow and contains in its axis a conical bony support, the *modiolus*, which tapers from a broad base to a pointed apex beneath the broader, blunt, and rounded *cupola* of the outer bony wall. The modiolus contains a broad canal which receives the cochlear division of the eighth cranial nerve as it enters from the internal meatus.

The outer surface of the modiolus supports a bony shelf, the *lamina spiralis*, which winds in a spiral manner from its base to its apex, and ends in a hook-like process, the *hamulus*. This shelf only partially spans the interval between the modiolus and the outer wall of the cochlea. In life the remaining interval is completed by a firm fibrous membrane, the *basal membrane* (*lamina basilaris*). Thus the cylindrical canal of the cochlea, which is wound spirally around the modiolus making two and one-half turns

from the base to the apex, is subdivided into two parallel longitudinal divisions, which are respectively known as the *scala vestibuli* and the *scala tympani*. They are so disposed that in a given turn of the canal the former is always nearer the apex, the latter nearer the base of the cochlea.

The bony lamina spiralis presents a grooved margin or *sulcus*, from the basal or tympanic lip of which the lamina basilaris is continued to the opposing surface of the bony wall. The bony lamina spiralis is hollowed out in a diploic manner for the transmission of the branches of the cochlear nerve, which are continuously given off all the way from the base to the apex of the spiral lamina, and which pass outward upon the basal membrane to be distributed to the epithelium of the *organ of Corti*. This organ is a peculiar spiral group of neuro-epithelial cells which extends the whole length of the basal membrane from the base to the cupola of the cochlea.

The margin of the osseous lamina spiralis is much thickened by the fibrous and epithelial tissues by which it is invested, so that a membranous sulcus of considerable depth is formed between the two lips (vestibular and tympanic lips) of the bony *sulcus spiralis*. This is further thickened by a marked elevation of fibrous tissue covered by columnar cells, from the outer margin of which a delicate membrane, the *membrana tectoria*, extends outward and overhangs the epithelium of Corti's organ. From the inner margin of this elevation, which is supported by the vestibular lip of the bony lamina, a delicate membrane, the *membrane of Reissner*, passes obliquely outward to the bony wall of the cochlea, and in transsections appears to cut off a corner of the *scala vestibuli*, thus marking off a triangular space whose base is formed by the outer wall of the cochlea, its sides by the membrane of Reissner and the basal membrane upon which rests the organ of Corti; its blunt apex is found at the *sulcus spiralis*. Since these membranes extend the entire length of the bony spiral canal of the cochlea, the space which is thus apparently cut off from the *scala vestibuli* must form a spiral canal, included between the *scala tympani* on the one side and the *scala vestibuli* on the other; this canal is the *scala media* or *cochlear duct*.

The *scala media* is an endolymphatic canal. At the apex of the cochlea it ends in a blind extremity which is known as the *lagna*; its opposite end forms a blind pouch between the fenestra rotunda and the fenestra ovalis, at the base of the cochlea, which is termed the *cæcum vestibulare*. The *scala media* is connected

with the saccule and utricle by means of the *canalis reuniens*, as described above.

The *scala tympani* and *scala vestibuli*, on either side of the *scala media*, extend spirally from the base to the apex of the cochlea. At the apex they are united by the *helicotrema*, a continuation of these canals which curves around the hamulus. At the base of the cochlea the two canals diverge, the *scala tympani* ending abruptly at the *fenestra rotunda*, which is closed by a fibrous membrane, clothed on its tympanic surface by the flattened epithelium of the tympanic mucosa, and on its cochlear surface by the epithelium of the *scala tympani*. The *scala vestibuli*, on the other hand, is continued backward into the vestibule, where it is in relation with the external surface of the saccule and utricle, and, since it is in contact with the outer wall of the bony vestibule, this portion of the *scala vestibuli* receives the opening of the *fenestra ovalis*, which is closed by the foot plate of the stapes. Corresponding to the relative positions of the *fenestra ovalis* and *fenestra rotunda*, the *scala vestibuli* in the first turn of the cochlea lies above the *scala tympani*, and being somewhat the longer it also extends farther backward.

Having traced the general form and relations of the several portions of the cochlea, we are now in a position to study more carefully the finer structure of its more important parts.

The membranous wall of the *scala tympani* and *scala vestibuli* is clothed by a layer of flattened endothelial cells, which rest upon a double layer of fibrous tissue. Thus the *tunica propria* also serves as a periosteum for the inner surface of the bony wall of the cochlea, and conveys the blood and lymphatic vessels. The *scalæ* are perilymphatic canals.

The membrane of Reissner is an extremely delicate structure which consists of a thin central *substantia propria*, covered on either surface by endothelium, that on the one surface being continuous with the endothelium of the *scala vestibuli*, that on the other with the endothelium of the *scala media*.

The outer wall of the *scala media* is lined by a continuation of the endothelium in that portion which adjoins the membrane of Reissner, and this rests upon a fibrous membrane similar to that which forms the walls of the other *scalæ*. Toward the attachment of the *membrana basilaris*, however, the tissue of the outer fibrous wall of the *scala media* is much thickened, and forms a dense ligamentous structure, triangular in shape as seen in a longitudinal section of the cochlea, which receives the insertion of the *membrana*

basilaris at its apex, and being, like the basal membrane, continued from the base to the apex of the cochlea, is known as the *spiral ligament*. Its dense fibrous bands radiate from the attachment of

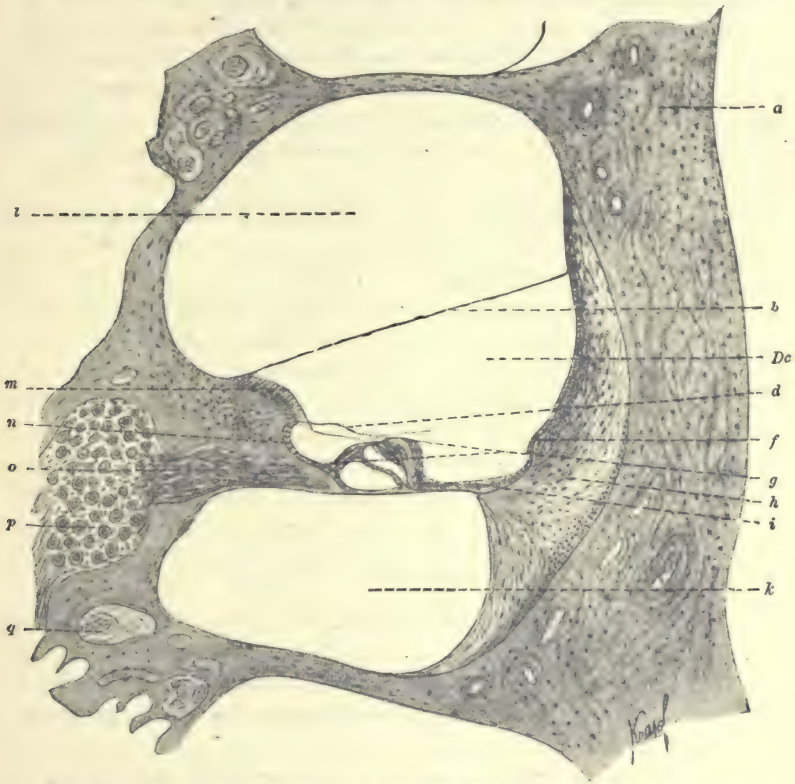


FIG. 456.—AXIAL SECTION THROUGH A TURN OF THE COCHLEA OF A GUINEA-PIG.

a, bone of the outer wall of the cochlea; *b*, membrane of Reissner; *d*, membrana tectoria; *Dc*, cochlear duct or scala media; *f*, stria vascularis; *g*, organ of Corti; *h*, spiral ligament; *i*, cells of Claudius; *k*, scala tympani; *l*, scala vestibuli; *m*, vestibular lip of the limbus spirale; *n*, spiral sulcus; *o*, nerve fibres of the cochlear nerve, contained within one of the radiating canals within the spiral lamina; *p*, nerve cells of the spiral ganglion; *q*, blood vessel. $\times 90$. (After Böhm and von Davidoff.)

the basal membrane to all portions of the ligament, and are firmly attached to the bony wall of the cochlea, with whose periosteum the deeper fibres of the spiral ligament are blended.

The surface of the spiral ligament, which forms the outer wall of the scala media, slopes gradually away from the attachment of the basal membrane; that which impinges upon the scala tympani

slopes more abruptly. The greater portion of the spiral ligament, therefore, is contained within the scala media. Here it is lined by low columnar or cuboidal epithelium whose cells blend, without demarkation, with the underlying vascular connective tissue, so that the minute blood vessels frequently appear as if lying within the epithelial layer, although they probably are always contained within the connective tissue processes which project into the attached surface of the epithelial layer. The middle of this area presents a prominent vascular ridge, which is known as the *stria vascularis*.

The tympanic wall or floor of the scala media presents for examination several structures, which, from within outward (viz., from the modiolus to the ligamentum spiralis), are the limbus spiralis, membrana tectoria, sulcus spiralis, basal membrane, and the organ of Corti which rests upon the basal membrane (Fig. 457).

The vestibular lip of the **limbus spiralis** presents a distinct elevation, which is formed by a peculiar cellular variety of connective tissue, and is covered by columnar epithelium, whose cells are not sharply defined from those of the underlying connective tissue. The surface of the epithelium presents a distinct cuticular formation of considerable thickness, which seems to be prolonged outward from the margin of the vestibular lip, and forms the membrana tectoria.

The surface of the limbus spiralis, when viewed from the scala media, presents slight elevations which, at the margin of the vestibular lip, are prolonged into prominent ridges whose indented borders overhang the sulcus and are known as the auditory teeth.

The membrana tectoria (*membrane of Corti*) is apparently an exoplasmic or cuticular tissue; although it presents a somewhat fibrillated appearance it contains no nuclei. Its free margin overhangs, or rests gently upon, the hair cells of Corti's organ.

The sulcus spiralis is a deep groove included between the vestibular lip of the limbus and the basal membrane which is attached to the tympanic lip. The sulcus is lined by flattened epithelial cells, which are apparently continuous with those of the vestibular lip, and like them are not readily distinguished from the underlying connective tissue. The epithelium is continued outward upon the basal membrane to the margin of Corti's organ, with the innermost cells of which it is continuous.

The basal membrane (*membrana basilaris*) is a thin but resistant membranous structure, upon which rests the epithelium of

Corti's organ. Its tympanic surface is clothed by a continuation of the lining membrane of the scala tympani, consisting of an endothelium, resting upon a very thin and delicate connective tissue layer. The substantia propria of the basal membrane consists of tendinous bands which, being radially disposed, span the interval between the margin of the tympanic lip of the osseous spiral lamina and the opposed margin of the spiral ligament.

Because of the great breadth of the modiolus at the base, and its rapid diminution in thickness toward the apex of the cochlea, this interval is relatively narrow at the beginning of the first turn of the spiral scala media, but progressively widens as the apex of the cochlea is approached. Consequently, the shortest tendinous fibres of the basal membrane are found at the base of the cochlea, the longest at its apex. The progressive increase in length of these fibres, as the scala media ascends its spiral course from the base to the apex of the cochlea, is one of the most significant facts which is disclosed by the minute anatomy of this complicated organ.

The substantia propria is covered upon that surface which faces the scala media by a thin homogeneous membrane, a cuticular formation or exoplasmic derivative, upon which rests the epithelium of the organ of Corti.

THE ORGAN OF CORTI consists of a highly differentiated neuro-epithelium whose specialized cells are disposed according to a very regular arrangement. The flattened epithelium of the sulcus spiralis is continued for a short distance upon the basal membrane. Suddenly, at the margin of Corti's organ, it alters its character. Here the epithelium becomes abruptly changed to a tall columnar variety, the first cells, known as the inner sustentacular cells, being apparently piled upon one another and resting against the inner hair cells, which form a single row of neuro-epithelium; these, like all the succeeding rows of cells, can be traced as a continuous line in the spirally wound scala media, from the base to the apex of the cochlea.

The inner hair cells have a broad body which is confined to the superficial third of the epithelial layer and which is nucleated at its deeper end. Its free surface forms an expanded oval plate from which about twenty cilia project through a cuticular membrane toward the cavity of the scala media. These end plates interdigitate with the phalanges of the inner pillar cells, which are to be shortly described. The bases of the inner hair cells are thin and slender, and are in relation with a nerve plexus of fine fibrils

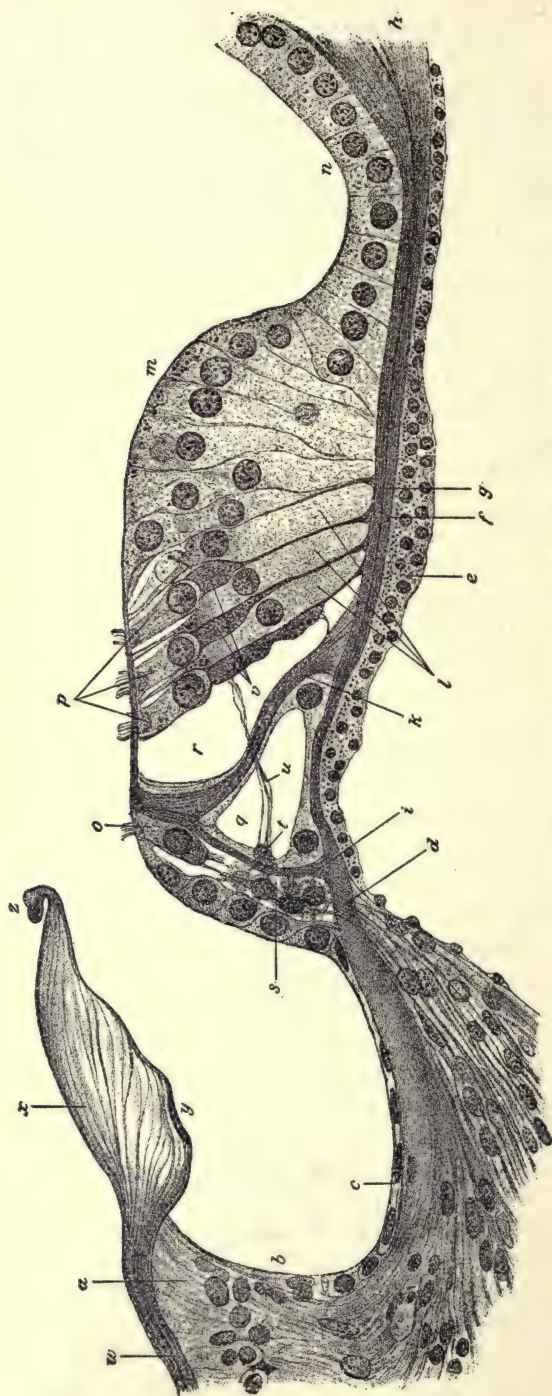


FIG. 457.—A RADIAL SECTION THROUGH CORTI'S ORGAN IN THE FIRST TURN OF THE HUMAN COCHLEA.

a, vestibular lip of the lamina spiralis; *b*, sulcus spiralis; *c*, epithelium of the sulcus; *d*, nerve fibres penetrating a foramen nervosum; *e*, epithelium of the scala tympani; *f*, fibrous layer of the basal membrane; *g*, outer hair cells; *h*, inner hair cells; *i*, tunnel; *j*, plexus about the outer hair cells; *k*, tunnel; *l*, plexus about the inner hair cells; *m*, Hensen's cells; *n*, cells of Claudius; *o*, inner, and *p*, outer hair cells; *q*, Corti's tunnel; *r*, Nuel's space; *s*, nerve plexus among the inner hair cells; *t*, plexus within the tunnel; *u*, tunnel fibres; *v*, plexus about the outer hair cells; *w*, *x*, *y*, *z*, membrana tectoria. $\times 465$. (After K  lliker.)

derived from the terminal processes of the cochlear nerve. These nerve fibrils make their exit in small bundles from the bony spiral lamina, and passing outward upon the basal membrane are distributed in a plexus beneath the epithelium, some of their naked processes almost immediately penetrating the epithelial layer to end between the bases of the inner hair cells.

The inner hair cells rest against the inner pillar cells of *Corti's arch*. This arch is formed by two rows of highly specialized cells, the *inner* and the *outer pillars*, which are widely separated where their bases are attached to the basal membrane, but are in contact at their free ends; in fact, the free extremity of the inner pillar is prolonged into a broad flattened plate-like process whose inner margin interdigitates with the head plate of the inner hair cells, as stated above, and whose outer margin is so prolonged as to almost, though not completely, cover the rounded head of the outer pillar. The head of the outer pillar, being similarly flattened, expanded, and prolonged outward beyond the margin of the head plate of the inner pillar cell, comes into contact with the phalanges of Deiters' cells and with the cilia of the outer hair cells which lie next without; they leave a space between the outer pillars and the outer hair cells which is known as *Nuel's space*.

The inner pillar cells are rather more numerous than the outer—in the entire length of the scala media, according to Retzius, there are 5,600 of the former to 4,000 of the latter—so that about three of the expanded head plates of the inner pillars overlap two of the rounded heads of the outer pillar cells. The arch formed by the opposed pillar cells, being succeeded by similar arches of successive pillars, forms a continuous tunnel, triangular in transection, which extends the whole length of the scala media, and is known as the *canal of Corti*.

Each pillar cell is differentiated into two portions, the pillar proper and the basilar cell, the latter containing the nucleus. The pillar presents a fibrillar appearance, the fibrils being disposed in the long axis of its body. This portion of the cell reaches from the basal membrane to the free surface of the neuro-epithelium.

The basal part of the cell, the basilar cell, probably represents the undifferentiated portion of the primordial pillar cell. It consists of a clear, finely granular cytoplasm and contains the spheroidal nucleus. It lies on that side of the pillar which faces the canal of Corti, the bases of the opposed cells being expanded until they meet, thus forming a cuticular floor for the tunnel. This

undifferentiated basilar portion occupies only the deeper half of the pillar cell.

The outer hair cells form three to five rows of ciliated cells which are similar in structure to the inner hair cells, and which are supported by the sustentacular cells of Deiters. Their cylindrical cell bodies occupy the superficial third of the epithelial layer and at the deeper extremity present a nucleated enlargement, beyond which they are continued only as a slender basal process. The free ends of the outer hair cells present an expanded oval surface from which the cilia project.

The outer sustentacular cells (Deiters' cells) are cylindrical cells whose expanded bases rest upon the basal membrane and whose distal portions extend toward the surface between the outer hair cells. The superficial portion of these cells, being encroached upon by the broad outer hair cells, is very slender; the broader basal portion occupies the deeper two-thirds of the neuro-epithelium, the spheroidal nuclei being found at the level of the middle third. Each sustentacular cell contains a *cuticular filament* which begins in contact with the cuticle of the basal membrane, and extends through the axis of the cell to its free border, where it expands to form a broad flattened plate of peculiar shape, known as the *phalangeal process*. These cuticular processes surround and overlie the margins of the head plates of the hair cells, thus forming a reticular layer through the openings of which the cilia of the hair cells project.

The cells of Deiters are succeeded by the sustentacular cells of *Hensen*, tall columnar cells about eight rows broad, the first of which equal in height the tall cells of the preceding type, but which at their outer border become abruptly shortened, pass into the cuboidal cells of *Claudius*, and are thus continued outward to the spiral ligament.

The nuclei of the cells of *Hensen* are found in their superficial third, those of the cells of *Claudius* in the center of the cell. Beneath *Hensen's* cells other small nucleated elements are occasionally found; they give to this layer somewhat the appearance of a two-rowed epithelium and are known as the cells of *Böttcher*.

Both the cells of *Hensen* and those of *Claudius* are provided with a cuticular margin which, with the similar cuticle of the cells of *Deiters*, forms a continuous, membranous, cuticular layer known as the *lamina reticularis*. The inner portion of this cuticular membrane is pierced by the cilia of the three to five rows of outer hair cells, as already described.

In the above description we have directed attention to the appearance of transections of the organ of Corti. In the study of this organ in the fresh condition, and occasionally in fixed and stained preparations, it is possible to obtain a surface view of this

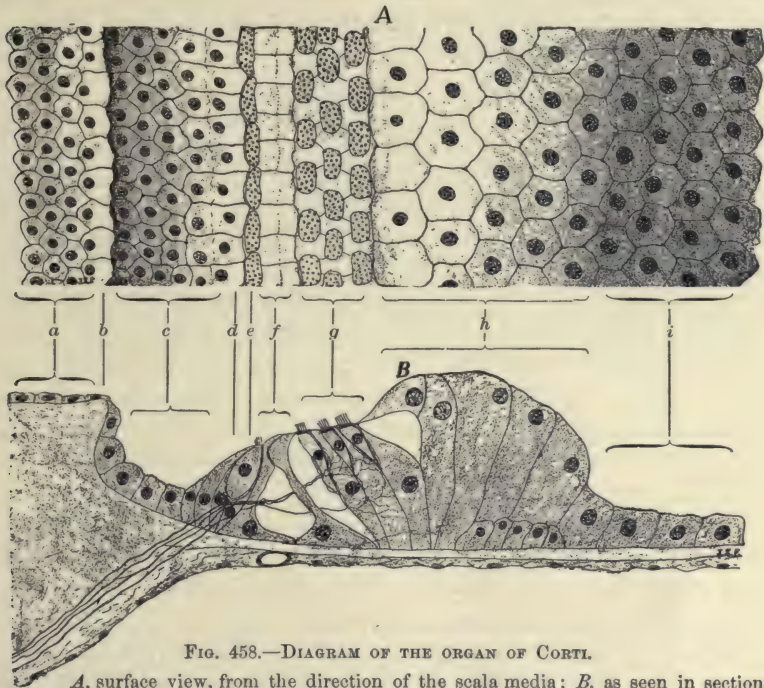


FIG. 458.—DIAGRAM OF THE ORGAN OF CORTI.

A, surface view, from the direction of the scala media; *B*, as seen in section, profile view. *a*, the vestibular lip of the lamina spiralis; *b*, margin of same; *c*, sulcus spiralis; *d*, inner sustentacular cells; *e*, inner hair cells; *f*, pillar cells; *g*, outer hair cells and phalanges; *h*, cells of Hensen; *i*, cells of Claudius. Very highly magnified.

organ from the direction of the scala media. In such preparations the polygonal outlines of the columnar cells of the limbus spiralis, beneath which are the auditory teeth, are seen on the outer side of the attachment of Reissner's membrane. Beneath the overhanging vestibular lip of the limbus the mosaic of large polygonal epithelial cells of the sulcus comes into view. At the margin of the organ of Corti these are exchanged for the broader cell ends of the inner sustentacular cells and the adjacent single row of inner hair cells.

The flattened rectangular head plates of the pillar cells form the next row, the heads of the outer pillars projecting from beneath,

and extending beyond the heads of the inner pillar cells. These are followed by the interdigitating phalanges of the cells of Deiters, which enter into the formation of the reticular membrane, through the fenestra of which the cilia of the three to five rows of outer hair cells project. This cuticular membrane is continued outward, and beneath it are successively seen the ends of the cells of Hensen, and of the cells of Claudius.

THE AUDITORY NERVE

The eighth cranial nerve presents two distinct divisions both of which are sensory, but which, as we have already seen, differ greatly as regards their central termination (see Chapter XXVI). They likewise differ in their peripheral distribution. Within the internal auditory meatus the nerve divides, each branch consisting of numerous bundles. The vestibular (superior or anterior) division is supplied with a ganglion of considerable size, the *ganglion of Scarpa*, beyond which the nerve separates into three branches which supply, respectively, the macula of the utricle, and the cristæ of the superior and external semicircular canals, in the neuro-epithelium of each of which their terminal fibrils end in relation with the bases of the hair cells (Figs. 452 and 453). The remaining nerve fibres which are distributed to the vestibule are derived from a branch of the cochlear (inferior or posterior) division, and they supply in a similar manner the macula of the saccule and the crista of the posterior semicircular canal.

The cochlear branch proper, cochlear nerve, enters the modiolus, where it becomes abruptly narrowed by giving off numerous fine branches which pass outward between the layers of the bony spiral lamina. Here they form a continuous spiral succession of small nerve trunks, supplied with many ganglion cells, which collectively form the *spiral ganglion* (Fig. 456). They penetrate the margin of the bony sulcus through the *foramina nervosa*, a succession of perforations, in the tympanic lip of the sulcus. Here the nerve fibres lose their medullary sheath and come almost at once into relation with the inner hair cells. From this point the path of the non-medullated fibres varies, most of them passing for some distance along a spiral course through the organ of Corti. One such spiral bundle is found on the inner, and another on the outer side of the inner pillars, the latter lying within the canal of Corti. Still other fibres, the *tunnel fibres*, cross the canal of Corti to form a spiral plexus beneath the outer hair cells and the cells of Deiters. Ter-

minal fibrils from these spiral plexuses end in relation with both the inner and the outer hair cells.

The relation of the nerve cells of the spiral ganglion and the ganglion of Scarpa to the termination of the nerve fibrils about the

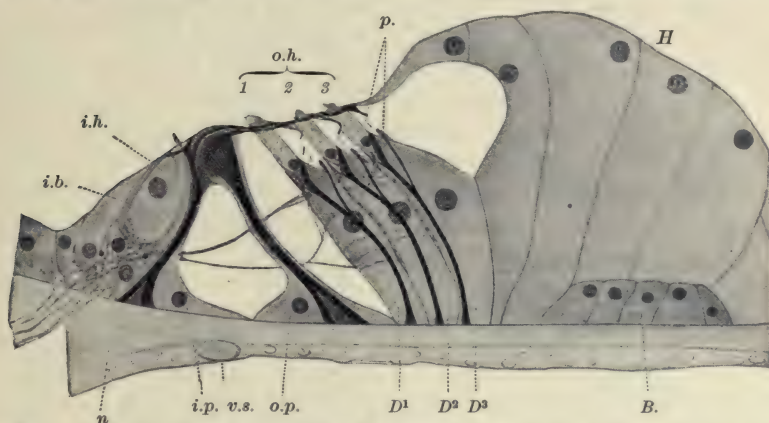


FIG. 459.—AXIAL SECTION THROUGH CORTI'S ORGAN OF THE GUINEA-PIG, SHOWING THE TERMINAL NERVE FIBRILS.

B., cells of Böttcher; *D¹*, *D²*, *D³*, three rows of Deiters' cells; *H*, cells of Hensen; *i.b.*, inner border cell; *i.h.*, inner hair cell; *i.p.*, inner pillar cell; *n*, terminal branch of the cochlear nerve; *o.h.*-1, 2, 3, three rows of outer hair cells; *o.p.*, outer pillar cell; *p.*, phalangeal process of the outer sustentacular process. Very highly magnified. (After Held.)

hair cells of the organ of Corti, the maculae, and the cristae, is essentially the same. The ganglia contain the cell bodies of the peripheral sensory neurones of the eighth cranial nerve. These are bipolar cells, of which the central process or neuraxis enters a medullated nerve fibre of the auditory nerve, while the peripheral process is distributed to the hair cells of the several areas of specialized neuro-epithelium, as above described.

BLOOD SUPPLY.—The internal ear is supplied by the internal auditory artery, which enters the labyrinth along with the auditory nerve, and at once divides into two main stems, the vestibular and the cochlear (*arteria cochlearis communis*, Siebenmann*). The vestibular branch accompanies the branches of the vestibular nerve to the saccule, utricle, and semicircular canals, supplying these structures in the posterior portion of the vestibule, and forming a rich plexus in the connective tissue of the maculae and cristae, and

* Handbuch der Anat., Bardeleben, Bd. v, Abth. II.

a more scanty network in the remaining portions of the membranous labyrinth.

The cochlear division of the internal auditory artery, according to Siebenmann, promptly subdivides into the cochlear artery

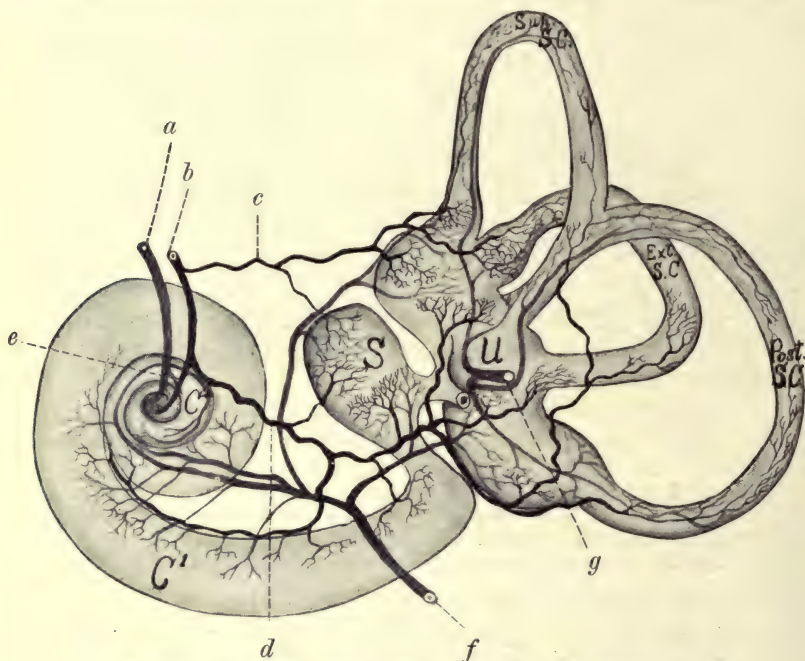


FIG. 460.—SCHEME OF THE VASCULAR SUPPLY OF THE INTERNAL EAR.

C, first turn of the cochlea; *S*, saccule; *Sup. S.C.*, *Ext. S.C.*, and *Post. S.C.*, superior, external, and posterior semicircular canals; *U*, utricle. The arteries are in heavy black, the veins somewhat lighter: *a*, central vein, and *b*, central artery of the cochlea; *c*, vestibular artery; *d*, vestibulo-cochlear artery; *e*, arteria propriae cochleae; *f*, vena aqueductus cochleae; *g*, vena aqueductus vestibuli.

proper, which appears as the continuation of the vessel, and the vestibulo-cochlear artery, which supplies the macula sacculi, the posterior ampulla, and the adjacent portions of the utricle and posterior semicircular canal. This vessel also supplies the early portion of the first turn of the spiral cochlea.

The true cochlear artery enters the modiolus and supplies a branch to the remaining portion of the first cochlear turn, and a terminal branch which passes as far as the apex of the cochlea, distributing its branches to the last two turns. All of these vessels are characterized by their peculiarly tortuous course. They dis-

tribute terminal branches to the limbus spiralis and to the connective tissue of the membranous scala vestibuli, extending as far around this canal as the spiral ligament. No vessels cross in the basal membrane.

The veins collect the blood from the limbus spiralis and the wall of the scala tympani and form venous trunks within the modiolus, which correspond more or less closely with the arteries. Those veins coming from the wall of the scala tympani unite to form anterior and posterior spiral veins in the limbus and inner wall of the scala tympani. These vessels chiefly empty into the vena aqueductus cochleæ which finds its way through the aqueduct to the internal jugular vein. Other branches from the interior of the cochlea unite to form the central vein of the cochlea, which

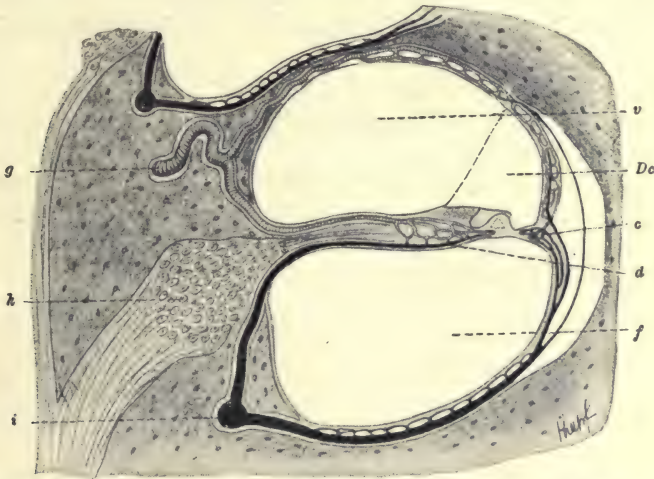


FIG. 461.—SCHEME OF THE VASCULAR TERMINATIONS IN THE WALL OF THE COCHLEAR CANALS.

c, capillary vessels in the spiral ligament; *De*, cochlear duct or scala media; *d*, capillaries in the limbus spiralis; *f*, scala tympani; *g*, arteriole; *h*, spiral ganglion; *i*, venule; *v*, scala vestibuli. (After Böhm and von Davidoff.)

becomes the chief radical of the internal auditory vein, and thus enters either the transverse or inferior petrosal sinus.

The veins from the utricle and semicircular canals mostly enter the vena aqueductus vestibuli, which follows its aqueduct to the superior petrosal sinus.

It will be perceived that the blood has three chief avenues of exit from the labyrinth: 1, by the vena aqueductus vestibuli; 2,

by the vena aqueductus cochleæ; and, 3, by the internal auditory vein. The greater portion of the blood pursues the second course and thus finds its way to the internal jugular vein, the smaller remainder entering the petrosal sinuses by one of the other two avenues.

LYMPHATICS.—The internal ear contains relatively few lymphatic vessels but is richly supplied with broad lymphatic spaces. Anastomosing vessels are found in the periosteum and membranous wall of the labyrinth. These communicate with the perilymph spaces between the periosteum and the membranous wall in the vestibule, and with the vestibular and tympanic scalæ in the cochlea. The perilymphatic spaces are connected with the subdural space of the meninges by means of lymphatic vessels in the aqueductus cochleæ. The perilymph of the vestibule also communicates with the subdural space through vessels which follow the sheaths of the nerves.

The endolymph cavities of the several divisions of the membranous labyrinth communicate freely with one another; by means of the ductus endolymphaticus a connection is also established through the aqueductus vestibuli with the subdural space, the blind terminal sacculus of this canal, the *sacculus endolymphaticus*, lying upon the posterior surface of the petrous bone and in contact with the dura mater.

CHAPTER XXX

TECHNIQUE

THE satisfactory examination of the tissues with the aid of the modern microscope requires certain preparatory steps which are at times very simple, at other times very complicated. The present chapter will deal very briefly with the more important of the simple methods and the general principles upon which they are based.

THE EXAMINATION OF FRESH TISSUES

Certain tissues may be examined immediately after they are removed from the body. This method is applicable to blood, lymph, scrapings from the spleen, liver, uterus, and similar organs, small bits of muscle, connective tissue, etc.

A small drop of blood may be collected upon the under surface of a cover glass, which is then quickly dropped upon a glass slide and examined at once. The glass must be thoroughly cleaned, otherwise a thin preparation can not be obtained. Slides and covers should be washed in very dilute hydrochloric acid, then washed in running water for several hours, and finally rinsed in 95 per cent. alcohol.

Scrapings from the epithelium of the mouth, or from similar mucous membranes may be prepared in the same manner as blood, and examined while still suspended in their own fluids. Most tissues, however, are not sufficiently well moistened for examination after this manner; the preparation must then be diluted with some inert fluid. Normal saline solution may be used for this purpose; the following formula is recommended:

Sodium chlorid..... 0.75 to 0.9 gm.

Distilled water..... 100 cc.

A 40 per cent. solution of glycerin in distilled water may be used for the same purpose; better still, the tissues may be suspended in a mixture of equal parts of alcohol, glycerin, and distilled water. The author has found this mixture to be especially

useful, for in it tissues may be kept for a long period without deterioration

THE DISSOCIATION OF TISSUES

It is frequently desirable to dissociate tissues, to a certain extent, into their component elements, prior to microscopical examination. This is accomplished by teasing, or by the solvent action of relatively strong acids or alkalis.

For **teasing**, minute bits of tissue are torn off by the aid of needles or scissors and carried to a clean slide, where they are to be kept always moistened with normal saline solution or other isotonic fluid. For their further manipulation a dissecting microscope is useful, though not essential. Two sharply pointed needles, mounted in wooden handles, are to be used.

The bit of tissue is pinioned with the needle held in the left hand, and with that in the right the tissue is gently torn by a rhythmic combing motion, being very careful to avoid squeezing the tissue between the needle and the slide. With a little practice bundles of fibres, groups of cells, etc., are readily separated sufficiently to be studied under moderate magnification. During the teasing, the bits of tissue should be kept well moistened, and are to be frequently inspected under low magnification to determine the progress of the operation. When satisfactorily prepared, a cover glass may be applied, and the preparation examined under higher magnification.

In *applying a cover glass* care should be taken to permit one edge of the cover to first touch the slide while being held at an angle of 30° to 40° . If the cover is then gently lowered into place, the air is forced out before the advance of the fluid, and the many air bubbles which would otherwise be included are not found in the preparation.

The method of teasing is particularly applicable to the study of the connective, and peripheral nervous tissues. White fibres, elastic fibres, fat cells, and nerve fibres are readily isolated in this way. If desired, they may be stained by the addition of a drop of a solution of methyl green, picro-carmin, etc.

Chemical Dissociation.—It is necessary to dissociate many tissues by chemical means, either because of the firm union of the elements composing the tissue or because they may be too delicate and fragile to withstand the mechanical teasing. Epithelial cells, nerve cells, and muscle fibres are readily prepared in this way.

For the dissociation of *muscle fibres* small cubes (0.25 to 0.5 cc.) are placed for ten to thirty minutes in the following solution :

Strong nitric acid..... 100 cc.

Potassium chlorate, sufficient to saturate.

The bits of tissue should be handled with glass rods. After some minutes they begin to disintegrate at the surface, and should then be transferred to running water, where they are left to wash for three to twelve hours. The pieces of tissue are then transferred to a mixture of equal parts of alcohol, glycerin, and water, and thoroughly shaken. Muscle fibres isolated in this way may be kept for months.

Epithelium may be dissociated by teasing or by the action of a 40 per cent. solution of potassium hydroxid, or by means of a 10 to 20 per cent. aqueous solution of "lysol," and preserved, if desired, in the mixture of alcohol, glycerin, and water.

For the isolation of *nerve cells* bits of the anterior horns of the spinal cord or other grey matter of the central nervous system may be treated in a similar manner. They may also be isolated by immersion in a 0.2 per cent. aqueous solution of "formalin" in normal salt solution for two to twenty-four hours (Gage *), or in a 0.2 per cent. aqueous solution of potassium bicarbonate, two to five days. Afterward they are transferred to a normal saline solution or to the mixture of alcohol, glycerin, and water, and isolated by shaking, assisted, if necessary, by gentle teasing.

Similar preparations may also be made by placing small bits of tissue in 30 per cent. alcohol for two days or more ; then shake thoroughly, allow the débris to settle, remove a drop of the fluid with a pipette, and examine.

Any of the above preparations may be stained by the addition of a small drop of a solution of eosin, picro-carmin, or methyl green to the fluid in which they are examined.

FIXATION

For the preservation of tissue, and as a preparation for further manipulation, most tissues require to be "fixed." Innumerable formulas have been advocated for this purpose, many of them having as their object the demonstration of certain structural features by the after application of special staining methods.

The action of the fixing fluids is in most cases dependent upon

* Vertebrate Histology, 1900.

the combination of the reagent with the chemical elements of which the tissue consists; very elaborate compounds are thus formed.

The following reagents are recommended for general use. The choice of a fixative is in great measure determined by the staining method which is to be afterward applied.

Alcohol.—This is especially useful for the fixation of the glandular organs. Tissue may be placed directly in 95 per cent., or in absolute alcohol. The fluid is to be changed in twenty-four hours, and again in five to seven days. This method of fixation is desirable for after staining the nervous tissues with methylen blue and for the demonstration of glycogen in the hepatic cells, cartilage, etc. Alcohol causes considerable distortion of the internal architecture of the cell by its rapid and forceful diffusion from the surface toward the center of the tissue, the cytoplasmic granules often being in this way forced to one side of the cell. This result may be partially avoided by the use of "*graded alcohol*," viz., 67* per cent. alcohol for three to twelve hours, 82† per cent. for twenty-four hours, and finally 95 per cent. alcohol, which should be once changed after a few days. Glycogen, however, is partially dissolved by the action of the dilute alcohols.

The distortion from the use of strong alcohol, as well as the dissociation which follows the use of the weaker strengths, may also be partially avoided by the addition of a little iodine to the stronger alcohol, or by combination with acetic acid, thus:

Glacial acetic acid.....	5 cc.
95 per cent. alcohol.....	60 cc.
Distilled water.....	35 cc.

After fixation for three to twenty-four hours the tissues are washed, and hardened by immersion for twenty-four hours in each strength of "*graded alcohol*," and may be kept indefinitely in 95 per cent. alcohol.

Tissues for fixation by this or any subsequent method are preferably cut into small cubes: a size not exceeding 0.5 to 1 cm. is most desirable. If larger pieces of tissue are necessarily used, the reagents will each require increased time to insure complete penetration.

Mercuric Chlorid.—This salt is to be used in saturated aqueous solution. As it dissolves with difficulty in cold water, the use of a hot, normal saline solution hastens the operation.

Mercuric chlorid is an excellent fixative for cytoplasm, but gives

* 95 per cent. alcohol, 3 parts; distilled water, 1 part.

† 95 per cent. alcohol, 5 parts; distilled water, 1 part.

still better results when combined with a nuclear fixative such as acetic acid. The following is an excellent method for general use :

Mercuric chlorid.....	7	gram.
Sodium chlorid.....	0.75	gram.
Distilled water.....	95	cc.

Just prior to use add 5 cc. of acetic acid.

Small pieces of tissue remain in this fluid for two to twenty-four hours, and are then transferred to graded alcohol (page 642), remaining twenty-four hours in each strength. Most dyes will act perfectly on tissue fixed in this way. If, however, the presence of mercury interferes with the action of a dye, this salt can be readily removed by the addition of a few crystals of iodine to the graded alcohol, renewing the iodine if necessary until it is no longer decolorized.

Formalin.—Tissues may be fixed in formalin or formol, a 40 per cent. solution of formaldehyde gas, which is to be used in strengths varying from 5 to 20 per cent. Small pieces should be left in the weaker solutions (5 to 10 per cent.) from six hours to two days, not longer. In the stronger solutions (10 to 20 per cent.) tissues should remain for only two to six hours. More prolonged immersion in the fixative causes considerable swelling. As a rule, the stronger solutions are preferable: this is especially true for the fixation of the cells of lymphoid tissue.

After fixation, the tissues are washed in running water for three to twelve hours and then hardened in graded alcohol. This method gives excellent results with lymphoid and epithelial tissues, but does not bring out the finer details of cytoplasmic structure.

Potassium Bichromate.—This salt has been used in all sorts of combinations; those which follow are to be specially recommended. Müller's solution is employed for the fixation of the tissues of the central nervous system, and must be used when fixation is to be followed by any of the Weigert hematoxylin staining methods. Applied to the fixation of other organs, Müller's fluid is apt to produce some maceration and better results are usually obtained with Müller-formol or with Tellyesniczky's solution.

For the special fixation of cytoplasmic granules, and also for after staining with Mallory's connective tissue stains, Zenker's solution yields the best results.

Müller's Solution :

Potassium bichromate.....	2.5	gram.
Sodium sulfate.....	1	gram.
Water.....	100	cc.

Pieces of tissue are left in the fluid for one to six weeks ; large pieces of the spinal cord or brain require four to six weeks. If left too long the tissues will become brittle. After fixation, the tissue is washed thoroughly in running water for twelve to twenty-four hours, and hardened in graded alcohol.

A relatively large volume of the fixing fluid should be used, and it should be frequently changed. It should not be allowed to become turbid nor to deposit crystals : this is avoided by frequent changes and by keeping the jars in the dark, or at least in such a position that they are not exposed to a bright light.

Tellyesniczky's Fluid :

Potassium bichromate.....	3 gm.
Glacial acetic acid... ..	5 cc.
Water.....	100 cc.

Pieces of tissue are placed in a considerable volume of the fixing fluid and left for three to seven days. They are then washed in running water for twelve to twenty-four hours, and hardened in graded alcohol. This fluid yields excellent results with muscular and glandular tissues, and is particularly serviceable where pieces of considerable size must be used, e. g., whole embryos.

Müller-Formol :

Müller's fluid.....	95 to 90 cc.
Pure formalin.....	5 to 10 cc.

This is an excellent fixative for general use, for by it most tissues are well preserved. Small pieces of tissue are left in a considerable volume of the fluid for one to five days, washed thoroughly in running water for twelve to twenty-four hours, and hardened in graded alcohol. The washing should be so thorough as to remove all excess of the chromium compounds, otherwise difficulty will be experienced in obtaining satisfactorily stained preparations.

Zenker's Solution :

Potassium bichromate.....	2.5 gm.
Sodium sulfate.....	1 gm.
Mercuric chlorid.....	5 gm.
Distilled water.....	100 cc.

Just prior to use add 1 cc. of glacial acetic acid to each 20 cc. of the fluid.

Small pieces of tissue, only, should be used. They remain in a considerable volume of the solution for three to twenty-four hours, after which they are thoroughly washed in running water for twelve to twenty-four hours, and hardened in graded alcohol. A

crystal of iodine should be added to the stronger alcohols until decolorization no longer occurs. If the mercury is not thus removed it will be difficult to obtain well stained specimens.

Flemming's Solution:

1 per cent. aqueous solution of osmium tetroxid	40 cc.
Glacial acetic acid.....	5 cc.
10 per cent. aqueous solution of chromic acid..	7.5 cc.
Distilled water.....	47.5 cc.

Pieces of tissue should not be more than 2 to 3 mm. in thickness and should be left in the solution and kept in the dark for one to twenty-four hours, according to the results desired. For mere fixation a short immersion is sufficient; for blackening fat and the myelin of medullated nerve fibres the longer period is necessary. After fixation the tissues are to be washed in running water for three to twenty-four hours, and hardened in graded alcohol.

This fluid gives excellent results for the fixation of the finer cytological elements of glandular epithelium, and serves to demonstrate the presence of fat and myelin, which are blackened by the osmium tetroxid. It does not penetrate the tissues very readily, and the surface of the piece is usually destroyed by overfixation.

Kleinenberg's Fluid:

Saturated aqueous solution of picric acid.....	99 cc.
Sulfuric acid.....	1 cc.

Shake well, filter, and dilute the filtrate with 200 cc. of distilled water.

Small pieces of tissue should be left in the fluid for about three hours and then transferred to 67 per cent. alcohol, which is changed two or three times during the first day. Hardening is continued in 82 and 85 per cent. alcohols, which are to be frequently changed. The picric acid will be slowly dissolved by the alcohol, but will not be entirely removed even after a considerable time; a trace remaining does no harm.

This fluid gives excellent results with small pieces of embryonic tissue, and possesses the additional advantage of removing the calcareous salts from partially calcified bone; it is not, however, a strong decalcifying reagent.

Van Gehuchten's Fluid:

Absolute alcohol.....	60 cc.
Chloroform.....	30 cc.
Glacial acetic acid.....	10 cc.

Very small pieces of tissue should be used. They should be left in the fluid three to twelve hours, and the vessel tightly closed to prevent evaporation of the volatile fluid. The tissues are then transferred to several changes of absolute alcohol to remove the fixing fluid and complete the dehydration.

This fluid can not be too highly recommended for the preservation of finer cytological details. It is not applicable to large pieces of tissue, and can be advantageously applied only to perfectly fresh, viz., living tissues.

Heat.—This is a useful agent for the fixation of blood, marrow cells, and scrapings from glandular and other organs, which are not to be afterward stained with methylen blue or its compounds. For this purpose smears made upon glass slides or cover glasses are quickly dried in the air, heated to 110° C. for twenty to thirty minutes, and are then ready for immediate staining.

The smears are made in the following manner: Slides or cover glasses should be thoroughly cleaned (see page 639) with a final rinsing in equal parts of absolute alcohol and ether. A small drop of blood or other fluid is collected by quickly touching the center of a cover glass to a drop of ordinary size. This cover glass is then immediately dropped upon the surface of a second one, and the two are drawn apart by a rapid sliding motion, the two surfaces being maintained parallel to one another during the motion. The success of the maneuver depends upon its rapidity, and to obtain very thin preparations some little dexterity is required.

Fairly good smears are more easily made with slides. A drop of blood is collected upon the end of one glass slide whose edge must have been ground. The end of the slide with the drop of blood is then touched to the middle of a second slide, the drop spreads out between the two, and the first slide is rapidly drawn over the surface of the second, while being held at an angle of about 45°. A broad smear is thus left upon the surface of the second slide, some portions of which are sufficiently thin, other portions too thick for use. Like the former maneuver the success of this depends upon rapidity, cleanliness, and the use of a sufficiently small drop of fluid.

Fixation by Vapors.—Smears of fluids or very thin pieces of tissue may be fixed by a very brief exposure to the vapor of osmium tetroxid, formalin, etc. This method is only useful in occasional instances.

In all methods of fixation where pieces of tissue are immersed

in the fixing and hardening fluids, it is desirable to prevent the distortion of the object from the pressure of contact with the glass container. This is accomplished by suspending the object by means of a thread, or by resting the tissue upon a thin layer of cotton placed in the bottom of the jar.

DECALCIFICATION

Tissues containing bone or other calcareous material require decalcification before they can be sectioned for examination. If the calcareous deposit is limited in amount, as in early fetal tissues, this can be accomplished and the tissue fixed at the same time by the use of Kleinenberg's fluid, a saturated aqueous solution of picric acid, or a 5 to 10 per cent. aqueous solution of sulfurous acid, the tissues being permitted to remain in the decalcifying fluid until a needle or slender scalpel can be readily pushed to the most central portions without producing great resistance or any grating sensation.

For well developed and mature bones the above methods are insufficient, and stronger acids must be relied upon. Nitric acid is the one most generally used for this purpose. The tissue should have been previously fixed, Müller-formol or mercuric chlorid being the preferable fixatives. The fixed and washed tissues are placed in 2 to 5 per cent. nitric acid, and the fluid changed daily until decalcification is complete. They are then thoroughly washed in running water for twelve to twenty-four hours and hardened in graded alcohol.

INJECTION

Injection is used either for the rapid dissemination of fixing fluids through whole organs, embryos, etc., or for the demonstration of blood or lymphatic vessels. For the former purpose mercuric chlorid is the most useful fixative, since it may be immediately followed by the injection of a hardening fluid, alcohol, by which the remaining mercury is dissolved out of the tissue before overfixation occurs. For the latter purpose a colored fluid, either aqueous or gelatinous, is forced into the blood or lymphatic vessels. Berlin blue, carmin, vermilion, and lampblack are the coloring matters most frequently used. The last two merely require suspension in a gelatinous or an aqueous menstruum; the preparation of Berlin blue and carmin is somewhat more complicated.

Berlin Blue Gelatin Mass:

Saturated aqueous solution of Berlin blue (Grübler's).....	100 cc.
Pure French gelatin (in sheets).....	5 to 10 grm.

The gelatin should be quickly washed to remove dust, etc., and then placed for several hours in a very little distilled water until it becomes swollen and soft. The superfluous water is then poured off, and the gelatin melted over a water bath. The warmed solution of Berlin blue may now be added, a little at a time, and continuously stirred. Finally, the mixture is filtered through cotton flannel which has been previously wrung out of hot water. If the mass is not to be used at once, a few crystals of thymol may be added as a preservative, or, after cooling, a little methylic alcohol may be floated upon the surface of the solidified mass. It is better to use it at once.

Carmin Gelatin Mass:

Carmin (Grübler's).....	3 grm.
Ammonium hydrate, strong.....	6 cc.
Pure French gelatin.....	7 grm.
Distilled water.....	80 cc.

The gelatin is prepared and melted as above, 50 cc. of the water being used, and the evaporation replaced. The carmin is rubbed up in a mortar with the remaining 30 cc. of the water, and the ammonia is added to render the carmin soluble. The mixture is now permitted to stand for two hours, after which it is neutralized by the gradual addition of 4 to 6 cc. of glacial acetic acid, the mixture being constantly stirred, and the latter portions of the acid diluted with four volumes of distilled water, and added drop by drop. The acid soon changes the color of the mixture from a purplish carmin to a bright crimson. Care should be taken not to add too much acid. When properly prepared, the sense of smell should detect both ammonia and acetic acid, and the fluid should have a dark crimson color (the addition of too much acid produces a brighter crimson). Should the mixture be slightly over-acidified a few drops of diluted ammonia will restore the proper condition. The carmin solution is now added to the gelatin mass, a little at a time and with constant stirring, and the whole is filtered through cotton flannel wrung out of hot water.

The gelatin mass may be kept for a short time by being covered with methylic alcohol, but is better used at once.

The pressure required for injection may be obtained by the gentle use of a hand syringe; by the displacement of the confined air in a large bottle or carboy by tap water; or much better by the use of a water blast, of which the small glass type is relatively inexpensive and will furnish a pressure for injection about equal to 180 mm. of mercury. The air outflow of the water blast is connected by rubber tubing with a glass canula of proper size to fit the vessel injected, a Wolff bottle containing the warm injection mass being interposed. If a manometer is connected, by means of a T-canula, on the proximal side of the Wolff bottle, a relatively even and accurately measured pressure is assured. The amount of pressure should be at first low (20 to 40 mm. of mercury), and should be gradually increased up to, but not much beyond, the normal blood pressure in the vessel injected.

The injected organ is cooled rapidly in a refrigerator, or by being packed in ice or immersed in ice water. After solidification small pieces are immediately placed in 95 per cent. alcohol for fixation, dehydration, and hardening.

HARDENING

After proper fixation nearly all tissues require to be hardened before satisfactory sections can be cut. This is accomplished by immersion in alcohol until dehydration is complete. The process requires from a day to a week, according to the size of the tissue and the volume and strength of the fluid. Various strengths of alcohol are advised. For general use the proceeding recommended by Gage* is found to be very satisfactory. The tissues after fixation are successively placed for one or two days in each of the following strengths of alcohol—67, 82, and 95 per cent. Tissues can remain indefinitely in the 95 per cent. alcohol, but are improved by being embedded for sectioning without great delay; this is especially true of tissue which has been fixed with Zenker's solution.

EMBEDDING

Thick sections may be obtained from the firmer tissues by free-hand sectioning with a razor, but for the satisfactory preparation of thin sections a microtome is a necessity and the tissues must be previously embedded to render them sufficiently firm. This is accomplished by infiltrating the tissue with celloidin or parafin, either of which yields a firm, waxy consistence.

* The Microscope.

Embedding in Celloidin.—Make a saturated solution of a little celloidin (Schering's) in a mixture of equal parts of alcohol and ether. The alcohol should contain no trace of copper sulfate. This solution is for convenience known as number III and should have a very thick, syrupy consistence.

A small portion of number III is mixed with three to five times its volume of the alcohol and ether mixture, to obtain number II, which should have a somewhat viscid consistence.

A second small portion of number III is diluted with ten to fifteen times its volume of the alcohol and ether, to produce celloidin number I, which should have a thin, watery consistence.

Small pieces of tissue which have been thoroughly hardened in 95 per cent. alcohol are treated as follows :

1. Dehydrate in absolute alcohol, six to twenty-four hours.
2. Place in the absolute alcohol and ether mixture, twelve to twenty-four hours.
3. Place in celloidin number I, twelve to twenty-four hours.
4. Place in celloidin number II, twelve to twenty-four hours.
5. Place in celloidin number III, twenty-four to forty-eight hours, or longer.

Pieces of tissue of considerable size may be satisfactorily embedded in celloidin, but should be passed through the successive solutions in a much more leisurely manner. Thus an eye requires two to three weeks, a large piece of the central nervous system three to four weeks for proper embedding. The tissue should now be fastened to a wooden block and the celloidin hardened. Ordinary wood yields its resins to the alcohol in which the blocks are to be kept; the white pine blocks which are commercially known as "deck plugs" contain very little resin and are admirably adapted for the purpose. The piece of tissue should now be properly oriented upon the block, the future sections being cut nearly parallel to the wooden surface. A bit of the thick celloidin is poured over the tissue; a few moments' exposure to the air firmly cements it to the block. As soon as the block can be inverted without dislodging the tissue, it is floated in a jar of chloroform, tissue down, for two or three hours. It is now ready for cutting, but if this is not done at once the blocks of tissue should be stored in a jar of 70 per cent. alcohol, in which they may be kept indefinitely. Stronger alcohol than 75 per cent. is apt to soften the celloidin and spoil the preparation.

Embedding in Paraffin.—If sections thinner than 15 μ are desired, paraffin embedding must be used; it is impossible to cut

celloidin sections with any great degree of certainty thinner than 10μ to 15μ . The paraffin method is also to be selected for the rapid preparation of tissues for sectioning, but it is only applicable to small pieces of tissue. For large pieces better results will be

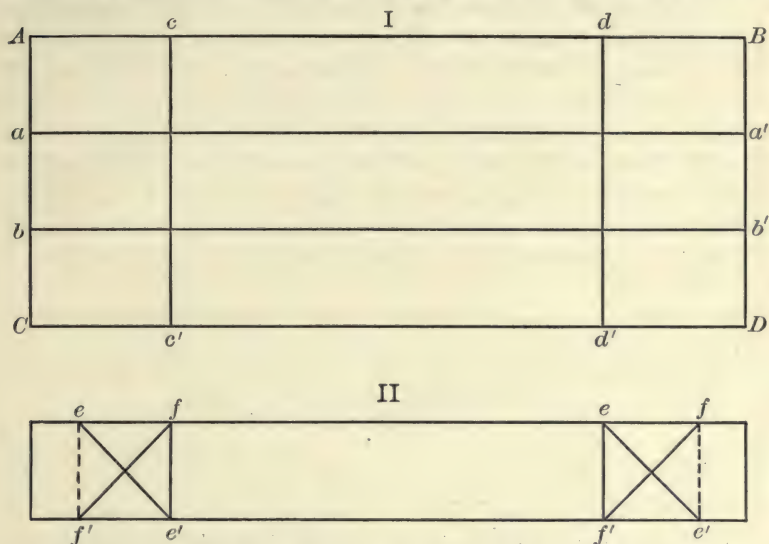


FIG. 462.—A METHOD OF PREPARING A PAPER BOX FOR PARAFFIN EMBEDDING.

I. A slip of paper, *A, B, D, C*, is folded, both ways, on the lines *a-a'*, *b-b'*, *c-c'*, and *d-d'*. Then being folded into the form shown in II, it is laid flat, the section *a, a', b', b'*, shown in I, being uppermost, and the paper is creased on the lines *e-e'* and *f-f'*. It is then opened, folded in the shape of a box, *f, e, f', e'*, forming the bottom, and is secured by folding down the ends after creasing the paper on the lines *e-f'* and *f-e'*.

obtained with celloidin. Many methods for the employment of paraffin have been extolled; the following can be recommended. The tissue, after fixation, should have been hardened in alcohol.

1. Dehydrate in absolute alcohol twenty-four to forty-eight hours; very small pieces of tissue (1 to 2 mm.) may be completely dehydrated in three to six hours.

2. Place in equal parts of absolute alcohol and xylol, one to three hours.

3. Place in pure xylol until clear and translucent, one-half to two hours. (For relatively large pieces of tissue cedar-wood oil or pure anilin oil may be substituted for the xylol.)

4. Place in melted paraffin containing a little xylol; that which has been previously used for embedding does very well.

5. Transfer to pure melted paraffin.

6. Transfer to a second dish of pure melted parafin. The object of these changes is to replace the xylol (or oil) with pure parafin. If the xylol is not completely removed the tissue will contain bubbles and satisfactory sections cannot be made.

7. Embed in a paper box or a watch glass. If glass is used the surface should be smeared with the least trace of glycerin to prevent adhesion. The box should be filled with pure melted parafin, the tissue handled with warmed forceps, and placed with proper orientation so that it is completely covered with the melted parafin. The parafin is now rapidly cooled by immersion in cold water; in summer months ice water must be used. If a paper box is used it can be left to float on the water until the parafin is thoroughly congealed. The manner of preparing these boxes is shown in Fig. 462.

Considerable depends upon the choice of a proper grade of parafin. That which melts at 58° to 65° is most desirable for use in temperate climates during the warmer months; during the winter months parafin of 54° to 56° is preferable. If too hard, the parafin cracks; if too soft, it fails to retain its form during sectioning. The former condition may be improved, if necessary, by the proximity of a small flame during the sectioning process, or by breathing upon the knife blade and tissue block; the latter fault may be remedied by placing the tissue for a short time in the refrigerator, just prior to cutting.

SECTIONING

The cutting of free-hand sections is so simple an operation as to scarcely require description. A small, inexpensive hand microtome and a sharp razor whose surfaces are ground flat, not concave, are all that is necessary.

For more precise sectioning a stationary microtome is a necessity. Many types of these instruments are on the market. The Thoma type of instrument is specially adapted for celloidin work, but may also be used for parafin sections. The Schanze instrument is very useful for celloidin sections and may also be used for small celloidin sections. The Minot rotary microtome is specially adapted for the production of serial sections in parafin. These instruments of themselves suggest the manner in which they are to be used, and the technique is easily acquired. Like all delicate instruments, they must be kept well cleaned and properly oiled, to do good service.

Much depends upon the choice and care of the knife. The microtome knives of Jung are of excellent quality and should be kept in good condition by the frequent use of the hone and strop.

The *hone* should be of fine Belgian stone. It should be well moistened with water, the addition of a little fine soap being a distinct advantage. The edge of the knife, carefully applied to the hone, should first be drawn obliquely from heel to toe and toward the operator, being held at a constant angle and drawn the whole length of the stone. The knife is then turned over and the motion is reversed, the knife being held obliquely at an angle equal to the previous one, the edge directed away from the operator, and the knife pushed from heel to toe, the whole length of the stone. The motion being repeated, a sharp edge is gradually acquired, which can be finished by the use of the strop.

In the use of the *strop* the motions are the reverse of those with the hone, the back of the knife in this case preceding its edge as it is drawn along the leather, and the draw should be from the toe to heel of the knife. The angle, however, between the knife and the hone and the knife and the strop should always be a constant one, and should be such that the microscopical "teeth" which are thus formed on the edge of the knife should be directed obliquely toward its heel.

In sectioning, the knife should be so placed in the microtome that its edge crosses the parafin embedded object at right angles, and for ribbon sectioning the parafin block should be so trimmed that it forms a perfect rectangle. In sectioning celloidin embedded objects, the knife should cross the object at as acute an angle as possible. With parafin, also, the stroke should be sharp and quick; with celloidin, somewhat slower and rhythmic. The knife should remain dry when used with parafin; with celloidin both the knife and the object should be at all times well moistened with 70 per cent. alcohol.

STAINING

The sections, having been cut, are at once ready for staining, provided they were embedded in celloidin. If parafin was used for embedding, the sections have first to be fastened to the slide. This is accomplished in the following manner.

The parafin sections are properly arranged upon the surface of a *clean* slide, a few drops of water from a pipette are allowed to flow between the slide and the sections, so that the latter float upon

the surface of the water; and the slide is gently heated over a small flame. Thus the parafin sections are straightened; care should be used not to melt them. The excess of water is now carefully poured off and the slide placed in an oven and heated to about 40° C. for several hours, until thoroughly dried. Most tissues will now adhere firmly to the slide. If, however, the tissue was fixed with solutions containing bichromate of potassium the sections are liable to come off the slide, a misfortune which may be avoided by the use of a celloidin adhesive, with or without the previous use of Mayer's albumin.

Mayer's Albumin :

White of egg, chopped with scalpel or
scissors, and filtered..... 10 cc.

Glycerin..... 10 cc.

Thymol..... a small crystal.

A drop of this fluid is to be diluted with eight or ten drops of distilled water and spread with a glass rod upon the surface of a clean slide. The excess is drained off, the slide inverted, leaned against the wall to protect it from dust, and allowed to dry in the air. The parafin sections are now placed upon the slide by the method detailed above.

Celloidin Adhesive.—The sections, having been fastened to the slide and dried, the parafin is removed by dipping the slide into one or two changes of pure xylol, the xylol removed by washing with absolute alcohol, and a few drops of very thin solution of celloidin (made by diluting thin celloidin, number I,* with eight or ten volumes of the alcohol and ether solvent) are poured over the sections. The solution of celloidin should be so thin as to scarcely leave an appreciable film on the slide. The excess of celloidin is drained off and the film hardened by first flooding the slide with 70 per cent. alcohol, and after a few minutes transferring it to water. The sections will not now be removed from the slide except by mechanical violence.

Celloidin sections do not need to be fastened to the slide before being stained; they are sufficiently firm to be gently handled with a needle.

Staining in Bulk.—It is occasionally desirable to stain tissue in bulk so that sections once cut can be immediately mounted. This is best accomplished by the use of a single stain applied to small blocks of tissue immediately after dehydration. Borax carmin is

* See page 650.

the most useful dye for the purpose, and is used as described below, except that it will require two or three days to penetrate the tissue.

Regressive Staining.—Staining in bulk is necessarily a regressive process, viz., the tissue is first overstained and then partially decolorized. With borax carmin the decolorization is accomplished by acid alcohol (hydrochloric acid 1 cc., 70 per cent. alcohol 100 cc.). Since the stain is removed more rapidly from the cytoplasm than from the nucleus, a differentiation is thus produced.

Progressive Staining.—In progressive staining the dye, having been once taken up by the tissue, is not removed, the differentiation of nucleus and cytoplasm being accomplished by the selective affinity of the dye. Thus, certain dyes are *nuclear*, others are *cytoplasmic*. The former possess a special affinity for the nucleus, the latter stain both nucleus and cytoplasm.

Certain dyes may be used either progressively or regressively; in the former case care must be exercised that the section be not overstained; in the latter case overstaining is impossible, but decolorization must be watched with care.

Classification of Dyes.—Dyes may be classified according to their affinity for certain granules or other portions of the cytoplasmic structure. A classification of this kind was advanced by Ehrlich through his pupil, G. Schwartz,* and has been greatly elaborated by Pappenheim.† Such a classification is very incomplete and unsatisfactory, but in a very general way serves a useful purpose. The following is sufficient for our present needs:

1. *Basic dyes*, those which color the chromatin of the nucleus and the so-called basophile granules. Hematein, methylen blue, methyl green, safranin, and basic fuchsin are examples.

2. *Acid dyes*, those which are usually cytoplasmic dyes, and have an affinity for the acidophile granules. Such are eosin, Congo red, orange G, methyl blue, and acid fuchsin.

3. *Neutral dyes*, which result from a due admixture of acid and basic colors, and which give a specific tint to the so-called neutrophile or azure granules. Such dyes are Ehrlich's triacid mixture, eosinated methylen blue, etc.

4. *Specific dyes*, which result from the due admixture of dyes with certain reagents, dyes or chemicals, and which have a selective affinity for particular tissues. This is an indefinite class which includes Weigert's elastic tissue stain, Mallory's connective tissue

* Inaug. Dissert., 1880.

† Grundriss der Farbechemie, 1901.

stain, Sudan III for fat, the intra vitam staining of nerve tissues with methylen blue, etc.

Mordants.—The successful application of a dye requires that the tissue shall have an affinity for the stain. This affinity may be either natural or artificial, e. g., eosin will color nearly all tissues under any ordinary conditions without the aid of any other reagent; hematoxylin, on the other hand, stains ordinary tissues but slightly, but its action is much enhanced by first acting upon the tissue with alum or a similar reagent. The alum, in this case, serves as a mordant.

A mordant should have a strong affinity for both the stain and the tissue. Hence it is that, after a tissue has been once stained by the aid of a mordant, it may be decolorized, partially or completely, by the second application of the same or another mordant of equal strength.

SINGLE STAINS WITH NUCLEAR DYES

Hematein.—Hematein is the active principle of the dye, hematoxylin, obtained by extracting logwood. Hematein is derived from solutions of hematoxylin by oxidation, either by chemical reagents or by prolonged exposure to the air. As a dye it must be combined with a mordant, which, most frequently, is some form of alum. The following formulas are recommended:

Alum Hematein (Mayer):

Alum hematein (Grübler's).....	0.2 grm.
95 per cent. alcohol.....	5 cc.
Saturated aqueous solution of ammonium alum	100 cc.

About 10 grm. of alum are required for this solution. The hematein should be first dissolved in the alcohol, with gentle heat if necessary, and afterward added to the warm solution of alum. The fluid is ready for use in two or three days, but will increase in strength for several weeks; it then requires dilution.

Böhmer's Hematoxylin:

Hematoxylin	0.5 grm.
Absolute alcohol	5 cc.
Saturated aqueous solution of potassium alum	100 cc.

The ingredients should be mixed as above and allowed to stand for eight to ten days in an open bottle. Filter. Ripening will continue for some weeks, and the dye will require dilution from time to time with a saturated solution of potassium alum.

Delafield's Hematoxylin :

Hematoxylin	4 gm.
95 per cent. alcohol.....	25 cc.
Saturated aqueous solution of ammonium alum	400 cc.

Mix as above and permit the fluid to stand exposed to the air and sunlight for three or four days. Add :

Glycerin	100 cc.
Methylic alcohol.....	100 cc.

After two days filter. After several days filter again. The fluid will ripen for several weeks and will require considerable dilution with a saturated aqueous solution of alum, containing glycerin and methylic alcohol in the above proportions.

This is a very deep nuclear stain, in fact it is so very deep that, while the nuclei are sharply differentiated, the intranuclear structure is nearly obliterated. The stain is somewhat improved in this particular by the slight regressive action of very weak acids—e. g., picric, or dilute acetic acid.

Mann's Acid Hematein :

Hematein (Grübler's).....	2 gm.
Absolute alcohol.....	100 cc.
Glycerin	100 cc.
Distilled water	100 cc.
Potassium alum	10 gm.
Glacial acetic acid.....	10 cc.

The hematein is dissolved in the acetic acid, with 25 cc. of the alcohol ; the glycerin and the remainder of the alcohol are then added. The alum is dissolved in water by the aid of heat, and the warm solution is poured into the solution of hematein. The fluid keeps indefinitely and is an excellent hematein stain for general use.

Application of the Hematein Stains.—All of the above solutions are used in a similar manner. Sections, either free or attached to the slide, are taken from water and immersed in the dye for three to five minutes ; they are then thoroughly washed in water. The stained sections are at first of a reddish-purple color, but soon become a deep blue from the slight alkalinity of the tap water used for washing. If necessary this alkalinity may be increased by the addition of one or two drops of ammonia to 500 cc. of the water used for washing.

Methylen Blue.—This dye is a derivative of thionin, and may be similarly used. For staining fresh tissues the dye is used in 2

per cent. aqueous solution. Its preparations are not very permanent. The chief uses of this dye are in combination with eosin as a stain for blood; as a stain for nerve cells according to the method of Nissl; and as applied to living organs as a specific stain for nerve tissues after the method of Ehrlich. These methods will be described below.

Methyl Green.—This dye is preferable to methylen blue as a stain for fresh tissues. It is used in 2 per cent. aqueous solution and applied as a progressive stain. It also enters into the composition of Ehrlich's triacid mixture. It is strongly basic.

Carmin.—This valuable dye is derived from the cochineal bug, and is used either as a progressive or a regressive stain. For the former, picro-carmin or alum carmin are recommended; for the latter, borax carmin is preferable.

Borax Carmin :

Borax	4 gm.
Distilled water (boiling) . . .	100 cc.; cool, filter, and add
Carmin	3 gm.; when dissolved, add
70 per cent. alcohol	100 cc.

Mix the ingredients in the above order, and after twenty-four hours filter. It may be necessary to use a drop or two of ammonia to complete the solution of the carmin. This is again removed by evaporation.

Tissues are to be overstained in the carmin solution, and differentiated in acid alcohol (70 per cent. alcohol containing 0.5 to 1 per cent. of hydrochloric acid) until the red color is no longer removed in clouds. The sections are then well washed with several changes of 95 per cent. alcohol, cleared and mounted.

Alum Carmin :

Potassium alum	5 gm.
Distilled water (hot)	100 cc.
Carmin	1 gm.

Mix in the order given, boil for twenty minutes, and when cold filter.

Picro-Carmin :

Ammonium hydrate	5 cc.
Distilled water	50 cc.
Carmin	1 gm.; when dissolved, add
Saturated aqueous solution of	
picric acid	50 cc.

Expose to light and air for two days; filter.

Picro-carmin is used as a progressive stain. Since the picric acid is soluble in alcohol, dehydration should be rapid, or a crystal of picric acid should be added to the alcohol used for dehydration.

Safranin.—This dye is a coal-tar derivative; it is an excellent nuclear stain. Like carmin, safranin yields a deep red color.

Safranin O (Grübler's)..... 1 grm.

Distilled water..... 100 cc.

1. Tissues taken from water are stained five minutes.
2. Wash in water.
3. Dehydrate rapidly in absolute alcohol. The alcohol removes some of the safranin, giving a regressive effect.

SINGLE STAINS WITH CYTOPLASMIC DYES

Eosin.—This dye is a coal-tar derivative. There are no less than seventeen varieties of the dye on the market, of which five are in general use. These are: (1) yellowish alcoholic; (2) bluish alcoholic; (3) yellowish watery; (4) bluish watery; (5) pure French eosin. The most reliable of these dyes are manufactured by Grübler. The first and fifth varieties are to be recommended as blood stains, the first and fourth are the best for general use. Two distinct methods are based upon this choice of dyes.

Method I:

Yellowish alcoholic eosin..... 1 grm.

70 per cent. alcohol..... 100 cc.

This stock solution is usually diluted with four to ten volumes of 70 to 95 per cent. alcohol just before using. The stain is preferably preceded by the use of a nuclear dye, after which the sections should be dehydrated in 95 per cent. alcohol.

1. Stain in the diluted eosin, one to five minutes, or until the sections become a bright red color.
2. Wash quickly in absolute alcohol, clear, and mount. The color is dissolved out during this process, producing some differentiation by regression.

Method II:

Bluish watery eosin..... 1 grm.

Distilled water..... 100 cc.

The stock solution should be diluted with one to four volumes of distilled water before using.

1. Tissues are taken from water and placed in the dilute eosin, one to five minutes.
2. Wash quickly in water to remove the excess of the dye.

3. Dehydrate in 95 per cent. alcohol, clear, and mount.

Slight differentiation may be obtained by prolonging the washing in water, otherwise the stain is progressive. Much greater differentiation is possible with either eosin method by making the stain very dilute and staining for twenty-four to forty-eight hours.

Congo Red:

Congo red 1 gm.

Distilled water..... 100 cc.

A few drops of dilute acetic acid should usually be added to the above; the bright red color is then exchanged for a dull bluish red, and in this neutralized condition the stain usually gives the highest differentiation. The dye should be used in the same manner as watery eosin (see *Method II*, above). Congo red gives especially good results when applied to fetal and young tissues.

Orange G.—There are many varieties of orange. The orange G and the aurantia of Grüber will be found satisfactory. As a cytoplasmic stain the former is preferable. It should be used in the same manner as alcoholic eosin (see *Method I*, above).

Fuchsin.—Two distinct dyes, the one of acid, the other of basic, properties, pass under this name. Acid fuchsin is a cytoplasmic dye, but when used in acid solution has a slight selective affinity for the nuclei. Basic fuchsin is chiefly useful in bacteriology. It is also used in preparing Weigert's elastic tissue stain.

DOUBLE STAINING

Hematein and Eosin:

1. Stain with one of the hematein solutions, preferably Mann's for general use, five minutes.

2. Wash well in water.

3. Stain in watery eosin, one to ten minutes. Or—

3. Dehydrate in 95 per cent. alcohol.

4. Wash quickly in water.

4. Stain in alcoholic eosin, one to five minutes.

5. Dehydrate in absolute alcohol.

5. Dehydrate quickly (one to five minutes) in absolute alcohol.

6. Clear and mount.

6. Clear and mount.

Methyl Blue and Safranin.—Methyl blue is a very different dye from methylen blue but is practically identical with water blue (Wasser blau). It is an acid or cytoplasmic stain.

1. Stain with a 2 per cent. aqueous solution of methyl blue, three minutes.
2. Rinse in water.
3. Stain in a 1 per cent. aqueous solution of safranin, five minutes.
4. Wash in water.
5. Differentiate and dehydrate quickly in absolute alcohol, till the sections become again blue.
6. Clear and mount.

This method gives a permanent stain which yields excellent results with certain tissues—e. g., the skin.

Other nuclear and cytoplasmic dyes may be combined in a similar manner to the above methods.

SPECIAL STAINING METHODS

Iron Hematoxylin (*Heidenhain*):**I. Mordant:**

Ferric alum (violet crystals).....	2 gm.
Distilled water.....	100 cc.

II. Stain:

Hematoxylin	1 gm.
95 per cent. alcohol.....	10 cc.
Distilled water.....	100 cc.

1. Mordant the sections one-half to two hours in I.
2. Rinse in water.
3. Stain ten to thirty minutes in II.
4. Wash well in water. The sections should become very black; a drop or two of ammonia to one-half litre of water often improves the color.
5. Decolorize in the mordant, watching each section, and stopping the decolorization at the proper time by—
6. Wash thoroughly in slowly running water, or in several changes of still water.
7. Counter-stain if desired, dehydrate, clear, and mount.

This method gives an excellent stain for the finer nuclear structure, mitosis, etc.

Muchematein (*Mayer*):

Hematein (Grübler's).....	0.2 gm.
Glycerin.....	40 cc.
Aluminum chlorid.....	0.1 gm.
Distilled water.....	60 cc.

Mix the ingredients in the order given, rubbing the hematein with the glycerin in a mortar. One or two drops of nitric acid added to the final mixture will sharpen its properties as a nuclear stain.

This dye is used as a specific stain for mucinous tissues. It is used in the same manner as hematein, and stains rapidly (three to ten minutes).

Mucicarmin (*Mayer*) :

Carmin.....	1	gram.
Aluminum chlorid.....	0.5	gram.
Distilled water.....	2	cc.
50 per cent. alcohol.....	100	cc.

Mix in the order given; heat over a small flame till the fluid darkens (two minutes); after twenty-four hours, filter. For use, dilute with five to ten volumes of 50 per cent. alcohol. Like muc-hematein, mucicarmin is a specific stain for mucus containing cells. It also stains rapidly.

Weigert-Pal Stain for Medullated Nerve Fibres.—The tissues must have been previously *fixed in Müller's fluid*, washed in water, hardened in alcohol, and sectioned.

I. *Stain* :

Hematoxylin.....	1	gram.
Absolute alcohol.....	10	cc.
Distilled water.....	90	cc.
Saturated aqueous solution of lithium car- bonate (1 to 80).....	1	cc.

II. *Differentiating Solution* :

Potassium permanganate.....	0.25	gram.
Distilled water.....	100	cc.

III. *Decolorizing Solution* :

1 per cent. aqueous solution of oxalic acid....	50	cc.
1 per cent. aqueous solution of potassium sulfite	50	cc.

This last solution should be freshly prepared by mixing the two stock solutions just prior to use.

1. Stain sections (six to twenty-four hours) until black.
2. Wash well in water. A few drops of lithium carbonate solution added to the water may improve the color, which should become a deep blue-black.
3. Differentiate until the grey matter becomes brown (one-quarter to two minutes).
4. Rinse in water.

5. Decolorize until the white matter becomes a steel blue, the grey matter a light brown (one-quarter to one minute), watching each section with care.

6. Wash thoroughly in several changes of water, or in running water.

7. If desired, counter-stain with alum carmin, and wash in water.

8. Dehydrate, clear, and mount.

Methylen Blue for Nerve Tissues (A, Intravital Method):

I. Stain:

Methylen blue (Grübler's "rectif. nach Ehrlich").....	0.1 grm.
Distilled water.....	100 cc.

Dissolve with heat, cool, and filter.

II. Fixing Solution (Bethe's):

Ammonium molybdate.....	1 grm.
Distilled water.....	20 cc.
Hydrochloric acid, C. P.....	1 drop.

The solution should be freshly made and kept at or near 0° C.

1. The method is only applicable to living tissues, by injecting the blood vessels with the stain, or by partially immersing in the staining fluid small pieces of tissue, freshly removed from the living animal.

2. After ten to thirty minutes, rinse in normal saline solution, and place in the cold fixing solution for two to six hours, according to the size of the pieces. The tissue should be kept cold.

3. Wash well in distilled water.

4. Dehydrate quickly in 95 per cent. and absolute alcohol, kept at or near 0° C.

5. Embed in paraffin. At a convenient time, cut and mount.

The stain is rather unstable, but may be kept fairly well if mounted in glycerin or in neutral balsam.

Methylen Blue for Nerve Tissues (B, Nissl's Method):

I. Stain:

Methylen blue (Grübler's "B pat.")...	3.75 grm.
Venetian soap (white Castile).....	1.75 grm.
Distilled water.....	1000 cc.

II. Differentiating Solution:

Anilin oil (pure).....	10 cc.
95 per cent. alcohol.....	90 cc.

This method is only applicable to tissue which has been fixed in 95 per cent., or in absolute alcohol. Thionin may be substituted for the methylen blue in the stain.

1. Warm the stain till steam begins to rise; then immerse the sections for four to six minutes. They acquire a deep blue color.

2. Rinse in distilled water.

3. Differentiate in the anilin alcohol till the sections become a light blue, carefully observing each section (twenty to sixty seconds).

4. Wash in 95 per cent. alcohol.

5. Clear in equal parts of origanum and cajuput oils, and mount in neutral balsam or in colophonium dissolved in xylol.

Eosinate of Methylen Blue (Hasting's Method):

For the somewhat complicated method of preparing the stain the reader is referred to the original article, Johns Hop. Hosp. Bull., 1904, vol. xv, p. 122. The stain is applicable to smears of blood, marrow, splenic cells, etc. When used with smears which contain traces of fat, a preparatory treatment with a 2 per cent. aqueous solution of sodium metaphosphate, which probably serves as a mordant, improves the staining properties. Otherwise the stain is applied without previous fixation.

1. Stain for one minute.

2. Dilute the stain with several volumes of distilled water, and continue the stain for five minutes, or until satisfactorily differentiated.

3. Wash with distilled water.

4. Dry and mount.

Golgi's Stain for Nerve Cells:

I. Mordant:

1 per cent. aqueous solution of osmium tetroxid..... 10 cc.

3½ per cent. aqueous solution of potassium bichromate..... 40 cc.

II. Silver Solution:

Silver nitrate (crystals)..... 0.75 grm.

Distilled water..... 100 cc.

This method is only applicable to fresh tissues, and the best results are obtained when the tissue is taken from a fetus or from an animal not over three days old. Thin slices or small bits of tissue must be used.

1. Fix in the mordant for ten days, frequently changing the

fluid, which should not become turbid, nor should its odor of osmium tetroxid entirely disappear.

2. Rinse quickly in water.
3. Place tissues in the silver solution, diluted with two volumes of distilled water, for fifteen minutes.
4. Place in the undiluted silver solution twenty-four to forty-eight hours. If several pieces of tissue are prepared they should be removed at intervals, as the duration of the impregnation by silver is always an experiment.
5. Dehydrate in absolute alcohol, one hour.
6. Transfer to equal parts of absolute alcohol and ether, half an hour.
7. Thin celloidin (number 1), thirty minutes.
8. Thick celloidin (number 3), thirty to forty-five minutes.
9. Transfer to a wooden block and fasten with celloidin.
10. Harden the celloidin block in chloroform, one-half to one hour.
11. Cut at once, the sections being $50\ \mu$ to $100\ \mu$ thick. While cutting, the knife should be well moistened with bergamot oil, not alcohol, and the sections, if not mounted at once, may be preserved for a short time in the same oil. Oil of lavender, cajuput, or origanum may be used in a similar manner.

Nitrate of Silver.—This reagent is used to outline epithelial cells by blackening the intercellular substance, the silver, after impregnation, being reduced or blackened by exposure to light.

1. The fresh tissue is immersed in a 0.25 per cent. to 0.5 per cent. aqueous solution of silver nitrate (crystals), and left in the dark for ten to twenty minutes.
2. Wash in distilled water, and while still in water, expose to direct sunlight until the object becomes a dark reddish-brown color (ten to thirty minutes).
3. Transfer to 70 per cent. alcohol, three to twelve hours.
4. Preserve in 95 per cent. alcohol.

Since nitrate of silver will attack metal instruments, the tissues while in this solution should be handled with glass rods. In silvering serous membranes, it is well to slightly stretch the object by tying it over a cork with a thread tightly fastened around the edge.

Gold Chlorid.—1. Wash the tissues in normal saline solution, and place them in pure lemon-juice until they appear clear (five to ten minutes).

2. Wash quickly in distilled water.

3. Place in the dark in a 1 per cent. aqueous solution of chlorid of gold for ten to forty-five minutes, according to the permeability of the tissue.

4. Wash in distilled water.

5. Place in a 25 per cent. aqueous solution of formic acid, and keep in the dark for twenty-four to forty-eight hours.

6. Wash thoroughly in water.

7. The tissue is now properly teased and mounted in glycerin, or sections may be dehydrated, cleared, and mounted in balsam.

The gold method is used for the demonstration of nerve plexuses and nerve terminations.

Picro-Fuchsin (Van Gieson).—This method is used as a specific stain for connective tissue; it colors the white fibres a bright red, all other tissues appearing yellow. Picro-fuchsin may be used as an after stain with nuclear dyes, e. g., hematoxylin, though the tissue must be greatly overstained with the nuclear dye, since the picric acid will decolorize hematein.

Saturated aqueous solution of picric acid.... 100 cc.

1 per cent. aqueous solution of acid fuchsin.. 5 cc.

1. Stain with Delafield's or Böhmer's hematoxylin, fifteen to thirty minutes.

2. Wash well with water. The sections should be almost black.

3. Stain with picro-fuchsin, three to five minutes.

4. Rinse quickly in water (water removes the fuchsin).

5. Dehydrate in absolute alcohol, clear, and mount.

Weigert's Elastic Tissue Stain.—This method gives a specific stain for elastic fibres; it may be used alone, or in combination with hematein and picro-fuchsin.

1 per cent. aqueous solution of basic fuchsin. 100 cc.

2 per cent. aqueous solution of resorcin..... 100 cc.

Boil the mixture in a porcelain capsule, and while hot, add liquor ferri sesquichloridi (Pharm. Ger., III), 25 cc.

Heat and stir for five minutes; a heavy precipitate is formed. Cool and filter. Dry the precipitate in a porcelain capsule over a water bath or sand bath. Dissolve the dried precipitate in 200 cc. of 95 per cent. alcohol, filter and replace the alcohol lost by evaporation. Add 4 cc. of pure hydrochloric acid.

Tissues should be stained twenty to sixty minutes, then thoroughly washed in water, dehydrated, cleared, and mounted.

The following method gives very beautiful results:

1. Stain in Delafield's or Böhmer's hematoxylin, twenty to thirty minutes.
2. Wash well with water.
3. Stain in Weigert's elastic tissue stain, twenty minutes.
4. Wash in water.
5. Stain in picro-fuchsin, three to five minutes.
6. Rinse quickly in water.
7. Dehydrate in absolute alcohol, clear, and mount.

Mallory's Connective Tissue Stain.—This method is applicable only to tissues which have been fixed in Zenker's solution and dehydrated with alcohol. Somewhat inferior results are obtained after fixation with mercuric chlorid.

I. Stain:

Acid fuchsin.....	0.1 gm.
Distilled water.....	100 cc.

II. Fixative:

Phosphomolybdic acid.....	1 gm.
Distilled water	100 cc.

III. Counter-Stain:

Anilin blue (soluble in water).....	0.5 gm.
Orange G (Grübler's).....	2 gm.
Oxalic acid	2 gm.
Distilled water.....	100 cc.

1. Stain in the fuchsin solution, three to twenty minutes. The sections should become a bright red.

2. Wash in water.

3. Fix in the phosphomolybdic acid solution, one minute. This prevents decolorization of the fuchsin.

4. Wash well in water.

5. Counter-stain in the blue solution, five to twenty minutes. The sections should become decidedly blue.

6. Wash in water.

7. Dehydrate, clear, and mount.

Eosin and Methyl Blue Mixture (Mann):

1 per cent. aqueous solution of <i>methyl</i> blue..	35 cc.
1 per cent. aqueous solution of bluish watery eosin	45 cc.
Distilled water.....	100 cc.

1. Mordant the sections in water, leaving them till all alcohol has been replaced (five to thirty minutes).
2. Stain in the above mixture, five to ten minutes.

3. Wash well and differentiate in water; the effect may be varied by the duration of the washing (ten to forty minutes).

4. Dehydrate in alcohol, clear, and mount.

When a sharper nuclear dye is desired the stain may be used as a counter-stain after hematein. In this case the methyl blue solution should be allowed to act only three to five minutes. The methyl blue used in this method is a cytoplasmic dye and should not be confounded with methylen blue.

Triacid Stain (Ehrlich) :

Saturated aqueous solution of orange G.....	13	cc.
Saturated aqueous solution of acid fuchsin..	7	cc.
Distilled water.....	15	cc.
95 per cent. alcohol.....	15	cc.
Saturated aqueous solution of methyl green.	12.5	cc.
95 per cent. alcohol.....	10	cc.
Glycerin.....	10	cc.

Be certain that the solutions of the dyes are saturated, and mix in the order given.

The following formula by *Mayer* may be substituted:

Distilled water.....	45	cc.
Glycerin.....	10	cc.
95 per cent. alcohol.....	25	cc.
Acid fuchsin.....	3	gm.
Orange G.....	2	gm.
Methyl green.....	1	gm.

Mix the fluids and dissolve the dyes in the order given.

When used for staining sections, either of these formulas should be diluted with five to ten volumes of the following mixture :

Glycerin.....	10	cc.
Distilled water.....	15	cc.
95 per cent. alcohol.....	25	cc.

1. Stain five to ten minutes in the diluted solution. (Use full strength for blood smears.)

2. Rinse in water.

3. Dehydrate in absolute alcohol. (Smears are dried in the air.)

4. Clear and mount.

MOUNTING

After staining, the sections are opaque; they must be rendered transparent for microscopical examination. This is accomplished by permeating the sections with oil; but since oil and water are

not miscible, the tissue must first be thoroughly dehydrated with alcohol. Immersing thin sections in 95 per cent. alcohol for three to five minutes is usually sufficient for this purpose unless xylol is to be used as the clarifying oil or unless the stain is injured by so prolonged an immersion. In either of these cases absolute alcohol is to be used for dehydration, because of its more rapid and thorough action.

Clarification.—Sections, either free or fastened to the slide, are immersed in oil until clear. Free sections will at first float on the oil, but when fully permeated will sink. Attached sections should lose all traces of “milky” appearance. The following oils are commonly used for clarification: Bergamot, origanum, cajuput, clove, carbo-xylol (pure carbolic acid, melted, 25 to 33 cc., xylol, 75 to 67 cc.), and xylol. Xylol is the most desirable in that it is perfectly miscible with the balsam in which the section is usually mounted, and is finally lost by evaporation. It will not act in the presence of the least trace of water. Carbo-xylol has the advantage of a slight affinity for water; this is also true of the heavier oils. Bergamot is desirable for celloidin sections, but has the disadvantage of rapid deterioration, after which it dissolves the celloidin. Either origanum or cajuput oil, or a mixture of the two, serves well for celloidin sections, but leaves them somewhat stiffer than does bergamot oil. The latter is therefore preferable for elastic tissues. On the whole, origanum serves best for routine work with celloidin sections, xylol or carbo-xylol for paraffin.

After clarification celloidin sections must be transferred to a slide. This is accomplished by means of a metal lifter or by a strip of rice paper (ordinary cigarette paper does nicely). The section, lying on the paper, is inverted upon the surface of the slide, to which it remains adherent after the paper is gently lifted. The excess of oil is then removed with blotting paper or by gentle pressure with a folded towel, a drop of xylol-balsam applied, and the cover glass dropped into position. The preparation is permanent.

Xylol-balsam is prepared by adding to Canada balsam sufficient xylol so that the mixture will have a thick, syrupy consistence, but will drop from a glass rod without stringing.

Sections may also be permanently mounted in *glycerin* without previous dehydration, the edge of the cover glass being, after some hours, covered with a ring of King's cement.

Neutral Balsam.—Sections may frequently be rendered more permanent by the use of neutral balsam, prepared as follows:

Dilute Canada balsam with xylol until it acquires a very thin watery consistence. Add sodium bicarbonate in excess. Shake thoroughly, and allow to stand in a stoppered bottle for twelve hours or more. Filter ; this is readily, though slowly, accomplished if the dilution is sufficient. Permit the solution to stand in an open vessel, protected from dust, until it evaporates to the proper consistence for use.

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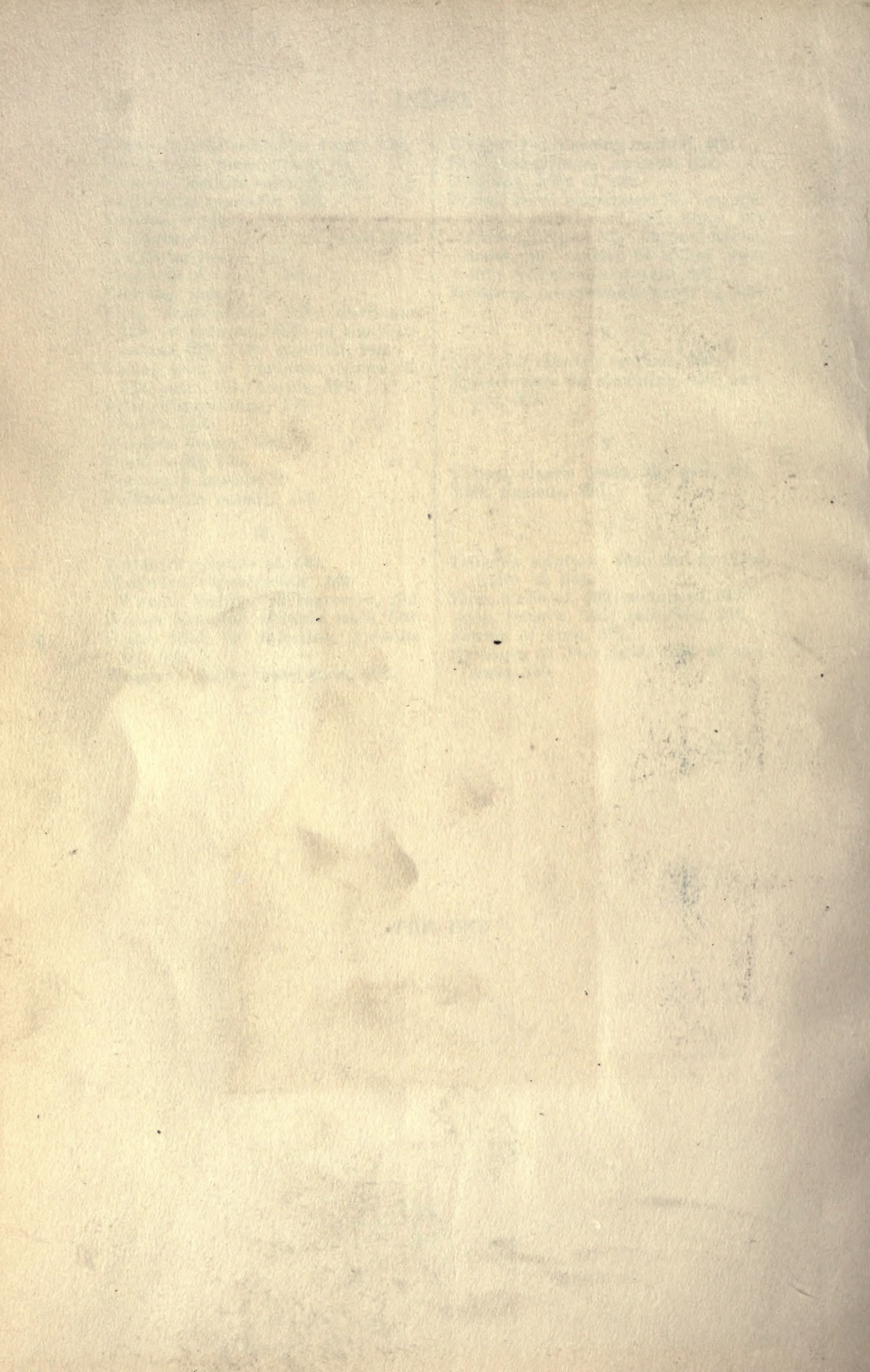
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